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INTUSSUSCEPTION—THE RELATION OF THE CEREBRAL CORTEX TO INTESTINAL MOTILITY IN THE MONKEY*

BY JAMES W. WATTS, M.D.,† AND JOHN F. FULTON, M.D.†

I Introduction

THE unexpected appearance of intussusception as a cause of death in a group of monkeys which had been subjected to bilateral removal of the premotor areas of the brain[10, 16, 17, 22] has necessitated examination of the etiology of intussusception, and it has led to a consideration of the influence exerted by the cerebral cortex on the motility of the gut. During the past three years careful autopsies have been performed in this laboratory on nearly three hundred monkeys and anthropoid apes of various species, almost all of which had been subjected at one time or another to surgical procedures on the brain or spinal cord (with intraperitoneal anesthesia), but intussusception had been observed in only three instances (see below, Autopsy V) in unoperated animals which had died obscurely, presumably from intestinal infestation.

In a recent investigation[16, 22] upon the functions of the premotor area some ten monkeys have had portions of their frontal lobes, including the premotor areas, removed from both hemispheres. Three of them died soon after the second premotor area was removed (see below, Autopsies I, II, III) with signs of intestinal obstruction, and at autopsy intussusceptions were disclosed. In several other instances, following premotor lesions, intussusceptions have been observed without obstruction. It is conceivable, though scarcely probable, that these occurrences were purely fortuitous, but they clearly merited close examination and the present paper records the results of our study.

The possible rôle played by the nervous system in the production of intussusception has often been discussed, but before taking up the question it is essential first to consider the mode of production of intussusception, i.e., the mechanical problem. The clearest description to be found in English literature, is probably that of Fraser[15], who wrote as follows:

"The mechanical process which results in the production of an intussusception is comparatively simple. It would seem that an irregularity in the conduction of the peristaltic wave is the underlying cause. A ring of contraction develops in a segment of the bowel, for some reason this is not transmitted, and its persistence at one point results in the invagination of the active portion into the lumen of the passive segment lying in continuity with it. The invagination of the advancing bowel results in a stimulation of the receiving portion, and this stage is actually the most critical of the whole process of intussusception, the contraction of the receiving bowel will have one of two possible effects—it will either expel the invaginating segment, in which case the danger has passed with no more symptoms than a passing colic, or, if its contraction has been longer delayed, it will grasp the entering segment, and actually force it along its invaginating course.

"While we may imagine the mechanical error to be somewhat on the lines described, there is difficulty in discovering the source of the original local peristalsis. It is probable that several factors are at fault.

"*Irritation of the mucous membrane has an influence on the production of the error.* . . . There is a structural peculiarity of the intestine which predisposes to the disease. . . . It is possible that an error in the arrangement of the splanchnic nervous system may influence the incidence of the disease. . . . There are cases of intussusception in which the inversion of a diverticulum, the presence of a polypus, or of a swollen hypertrophied Peyer's patch is the original stimulating factor of the peristalsis."

Fraser[15] mentions the possibility of an error in arrangement of the splanchnic nervous system being a factor in intussusception, and while the suggestion is frequently seen no experimental study of the problem appears to have been made, and certainly there is no record in the literature of an intussusception produced by peripheral stimulation of any of the nerves to the gut.

Clinically intussusception is one of the commonest and most dangerous causes of intestinal obstruction, but it is almost entirely confined to children under five years of age (Homans[19]). Perrin and Lindsay[35] observed that 69 per cent in their series of intussusceptions were in infants under one year of age. Intussusception

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occurs twice as frequently in boys as in girls, and is more common in well nourished than in malnourished children (Ochsner[30]). It is extremely rare in adults, in whom, however, it may be initiated by the drag of a pedunculated benign or malignant tumor (Homans[19]).

II Protocols of Autopsies

Soon after beginning a study of the effects of localized lesions in the hypothalamus on the heart and the gastrointestinal tract it became obvious that an accurate knowledge of the normal variations in the gastrointestinal tract of primates must be obtained (Watts and Fulton[10]). For this purpose one of us (J. W. W.) performed complete autopsies on all animals that were sacrificed or died during the year, some 80 in number, devoting special attention to the gastrointestinal tract. It was while making these routine examinations that interest was aroused in the problem through the discovery of intussusception with obstruction in several monkeys from which the premotor area had been previously extirpated.

These instances may be described briefly as follows:

Autopsy I (Frontal IV). Adult male Java monkey (Macaca irus). Following cortical extirpation, vomiting and prostration developed. Intussusception found at autopsy.

Previous Operations—July 5, 1932. Both frontal lobes including most of the premotor areas were radically ablated.

October 10, 1932. The remaining cortical tissue anterior to the central sulcus was extirpated from the left hemisphere. There were no gastrointestinal symptoms after either operation.

November 17, 1932. The remaining cortical tissue anterior to the right central sulcus was extirpated.

Following the last operation the animal was unable to sit or stand alone, and it had to be fed. Its general condition and appetite were good until the sixth day after operation when it suddenly became prostrated and vomited. The vomiting continued for several hours and was associated with coarse lateral nystagmus. The operative incision was well approximated; there was no evidence of infection, or of increased intracranial pressure. As it was evident that the animal could not live through the night it was sacrificed under dial anesthesia on the sixth day after operation.

Autopsy findings (November 23, 1932)—Upon opening the abdomen an intussusception 8 cm. long was discovered in the small intestine 42 cm. below the pylorus (Fig. 1). The mesentery had been dragged into the intussuscipiens with the intussusceptum. There was a disturbance of blood supply to the intestine indicated by the marked discoloration of the intestine at the site of and below the obstruction.

The intussusception had produced an intestinal obstruction with an interference of the blood supply to the bowel. This was adequate cause for the prostration and vomiting which were observed. The next two cases are similar, but case 3 is complicated by the presence of a spinal transection.

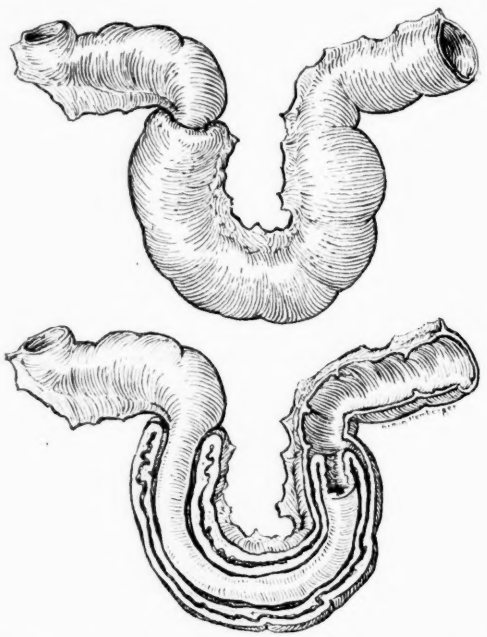

FIG. 1. (Autopsy I.) A drawing of the obstructive intussusception disclosed in Autopsy I as it appeared externally (above) and after dissection (below).

Autopsy II (Area 6 Series, No. 1). Adult Macaca mulatta. Weight 3800 gms. Intussusception found in animal following bilateral extirpation of motor and premotor areas of the cortex.

Previous Operations—January 5, 1933. After faradic stimulation of areas 4 and 6 of the left hemisphere, area 4 was extirpated.

January 26, 1933. The left bone flap was reëlevated, area 6 was stimulated and then extirpated.

February 9, 1933. Through a right-sided bone flap, the motor and premotor areas were stimulated, then excised. As usual after removal of the second motor and premotor areas, there was an absence of voluntary power in the contralateral and ipsilateral extremities.

The condition of the animal was good for several days after operation. Although the appetite was good, and it was carefully fed by hand, the animal lost weight. On February 15, it refused food and the following morning was found dead in its cage. No signs of an acute nature such as were observed in the previous case (Autopsy I) were noted in this animal. There was no vomitus in the mouth or on the face.

Autopsy findings (February 16, 1933)—An intussusception was found in the lower ileum 10 cm. from the cecum. The intussusception measured 2 cm., the mesentery had been pulled in with the intussusceptum, and there was some discoloration

of the intestine at the site of the obstruction and below it. The intestine for 3 or 4 cm. above the obstruction was definitely constricted, that below, dilated.

The discoloration of the intestine at the site of the obstruction indicated that the intussusception was present before death. That it was recent, was shown by the relatively slight disturbance of blood supply and by the presence of a constricted gut above the obstruction. Of course, it is possible that reduction of the intussusception might have occurred spontaneously had the animal lived.

Autopsy III (Corpus callosum IV. Intussusception XII). Mature male green monkey (Cercopithecus sabaeus aethiops). Weight 3200 gm. Intussusception found in animal following removal of the left motor and premotor area.

Previous operations—February 3, 1933. The left motor and premotor areas were extirpated.

March 9, 1933. The corpus callosum was transected.

March 22, 1933. A total transection of the spinal cord was made at the level of the 10th thoracic segment. Following the last operation, the general condition of the animal grew worse. A pressure sore developed over the left hip, so it was sacrificed March 31, 1933.

Autopsy findings (March 31, 1933)—The stomach was dilated and the intestines were atonic and somewhat distended. In the small intestine 40 cm. below the pylorus was an intussusception 3 cm. long. The loops of gut below the obstruction were definitely darker in color than the loops above it. The lower part of the intussuscipiens was also discolored. The blood vessels in the wall of the intestine above and below the obstruction were very prominent, and especially below there was a diffusion of blood into the mucosa radiating out from the blood vessels.

No inflammatory changes were present in the gastrointestinal tract of the preceding cases (Autopsies I, II, and III), nor was there any local abnormality which might be pointed to as the possible cause. There was a disturbance of the blood supply to the intestine below the site of obstruction in all three animals, and it is clear that the obstruction was a contributing, and probably, the chief cause of death. The following case (Autopsy IV) is that of an animal which had a stubborn diarrhea before it was operated on, and was subjected to an experiment in carbohydrate metabolism subsequently.

Autopsy IV (Area 6 Series, No. XX). Immature female Macaca mulatta. Weight 1800 gm. Intussusception found after operation on area 6 in animal which previously had diarrhea.

Previous operations. This young macaque had a stubborn diarrhea which failed to respond to treatment before an experiment was performed. On March 8, 1933 a small area, 2 mm. in diameter, was excised from the anterior end of the superior precentral sulcus of the left premotor area.

March 20, 1933. The animal was isolated, given water but no food, and injected daily with phloridzin for an experiment in carbohydrate metabolism. On March 22, a reddish fleshy mass was observed protruding from the rectum.

Autopsy findings (March 22, 1933)—The animal was sacrificed under ether anesthesia. When the abdomen was opened, an intussusception of the descending colon was found. The intussusception was composed entirely of descending colon including the mass protruding from the rectum. The intussuscipiens was largely rectum, though the upper 1 cm. of it may have been colon. The mucosa of the small and large intestines was slightly pinker and more injected than normal.

Fortunately, during the year, two unoperated animals were found to have intussusception at autopsy. If these had not occurred it might have been a temptation to neglect other factors concerned in the etiology of intussusception and to overstress the influence of the central nervous system. One animal (Autopsy V) presented evidence of a generalized infectious process and marked inflammatory changes in the gastrointestinal tract. No predisposing cause of the intussusceptions could be found in the other animal (Autopsy VI).

Autopsy V (Normal green, III). Cercopithecus sabaeus aethiops. Weight 3000 gm. Intussusception in unoperated animal that died of a generalized acute toxic process.

Past history. This was an unoperated animal which had recently arrived in the laboratory. No detailed observations had been made but it was noted that the monkey was not so active and alert as its fellows. The morning of June 17 it was found dead in its cage.

Autopsy findings (June 17, 1933)—The great omentum was very hemorrhagic in appearance, especially near the blood vessels. The parietal peritoneum contained many diffusely scattered punctate hemorrhages. The visceral peritoneum was also the site of punctate hemorrhages. The intestinal wall was a pea-soup green, having been discolored by the fecal contents. Considerable gas was present in the intestines.

Further examination disclosed 2 intussusceptions near the junction of the middle and upper third of the small intestine. The more cephalad intussusception was 5 mm. in length and the more caudal was 20 mm. long. Possibly the discoloration below the second intussusception was greater than that above, but the difference was very slight.

The fecal contents had the appearance and consistency of pea soup. The intestinal mucosa was swollen, velvety and assumed the color of the feces. A few scattered fresh hemorrhages were noted in the mucosa.

The spleen was swollen and firm to palpation. On cut section it had a septic appearance. The kidneys were swollen and flabby. Pus was present in the left kidney pelvis.

Autopsy VI (Normal green, V). Cercopithecus sabaeus aethiops. Weight 2575 gms. Intussusception in unoperated animal.

Past history. This was an immature male green monkey, which had arrived in the Laboratory ten days previously. During the two or three days preceding death it had appeared sick; did not jump about the cage as usual when food and water were placed before it by

an attendant. It was found dead in its cage the morning of July 1, 1933.

Autopsy findings (July 1, 1933)—When the peritoneal cavity was opened, an excessive amount of free fluid was present. There was an intussusception of the ileum through the ileocecal valve into the cecum. The intussuscipiens measured 12 cm. In the ascending colon was an intussusception measuring 7 cm. with marked discoloration of the involved segments as well as the bowel below the obstruction. A third intussusception was present in the descending colon, 8 cm. long, likewise with marked circulatory disturbances at the site and below the obstruction. The mucosa of the rectum was normal in color and appearance. There was no evidence of a generalized enteritis or colitis.

III Cortical Stimulation

Though suggestive the first three autopsies described above would in themselves allow no definite conclusions, and we were therefore led to investigate the effect of cortical stimulation on gastrointestinal motility. That cortical stimulation influences peristalsis has been known since the classical experiments of Bochefontaine[8] in 1876. He found that stimulation of the region of the sigmoid gyrus of the dog usually diminished or completely inhibited rhythmic contractions of the stomach. However, the inhibition was often immediately preceded by a strong peristaltic contraction of the entire pyloric region. Sometimes peristalsis was excited in various segments of intestine, now in the duodenum, again in the ileum.

The subjects of most of our experiments were monkeys having previous intracranial operations, which were to be sacrificed to obtain the brain for anatomical studies. This accounts for some of the apparently bizarre procedures antedating the present experiments. Such animals, however, were often of more value than a normal animal in analyzing the results, since they allowed more precise localization of excitable areas.

Methods.—After the cortex had been exposed the peritoneal cavity was opened. The cortex was kept moist with warm, physiological saline. In the earlier experiments the intestines were kept moist by sprinkling them with saline, but in later experiments, the animal was placed in a saline bath at 38° C., so that the intestines were largely immersed in saline, sometimes floating somewhat, depending on their gaseous content. The temperature of the fluid was kept constant by means of an electric light bulb.

In Experiments 1, 7, 8, 11, 12, and 13, the cortex was stimulated with a unipolar electrode with the indifferent electrode in the rectum. To avoid the possibility of stimulation from the indifferent electrode or the criticism its use might cause, in Experiments 2, 3, 4, 5, 6, 9, and 10, the cortex was stimulated by means of a bipolar electrode. Using a Harvard inductorium, the best results were usually obtained with the coil at 9 or 10 cm. The points most frequently used for stimulation in the various experiments are indicated diagrammatically by arabic numerals in figure 2.

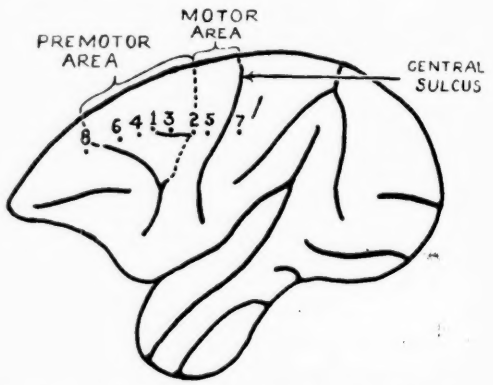

FIG. 2. Diagram of the cerebral hemisphere of a monkey showing the points stimulated. This applies to all experiments (1 to 13).

Experiment 1 (Corpus Callosum V. Intussusception I). Mature Macaca mulatta. Weight 3450 gm. Intussusception in small intestine and vigorous activity in cecum produced by faradic stimulation of premotor area.

Previous operations—February 17, 1933, the main trunk of the anterior cerebral artery was ligated at the genu of the corpus callosum, and the callosum sectioned. No impairment of motor function followed. The animal had diarrhea which failed to respond to treatment.

Observations upon intestine—March 24, 1933. Under ether anesthesia the left bone flap was reëlevated and the peritoneal cavity opened. The blood vessels in the intestinal walls were considerably injected. Observations from 9:40 to 10:00 A.M. showed very slight peristaltic movements of the small intestines, but none in the stomach or large intestine. Throughout the experiment the intestines were kept moist by sprinkling them with normal saline at 38° C.

10:20 A.M. With the coil at 10 cm. Point 1 (Fig. 2) was stimulated for 1 minute with a unipolar electrode with the indifferent electrode in the rectum.

20″ after the application of the electrode to the cortex the cecum began to contract. A bud-like evagination formed on the lower end of the cecum. As contraction of the musculature continued, the bud constricted at the base 1 cm. from the tip.

40″ after application of the electrode to the cortex, a narrow ring-like band of contraction was seen circumscribing the small intestine. The band gradually widened from 1 to 2 mm. and finally to 10 mm. The band remained contracted and was not transmitted down the gastrointestinal tract. A peristaltic wave arising

in cephalad segments reached the contracted segment but did not pass it.

10:30 A.M. With the coil at 10 cm. Point 2 was stimulated for 1 minute.

30″ after stimulation was started, a bud was seen forming at the lower end of the cecum.

50″ the bud was growing in size. This was associated with a slight general contraction of the entire cecum.

60″ a narrow band of contraction was seen in the small intestine and was not transmitted. At this time the evagination on the cecum measured 10 mm. long and 8 mm. in diameter.

10:34 A.M. The cecum had been slowly contracting and relaxing since the cortex was stimulated at 10:30, a cycle lasting about 2 minutes.

10:35 A.M. All was quiet.

10:36 A.M. With the coil at 10 cm., Point 3 was stimulated faradically 3 minutes.

20″ after stimulation was started, a band of contraction made its appearance 15 mm. from the lower end of the cecum.

30″ contraction of the cecum continued.

50″ a second constricting band appeared on the cecum proximal to the first.

70″ a narrow ring-like band was noted circumscribing the small intestine, which was not transmitted.

90″ a peristaltic wave arising above passed caudally, broke against the narrow contracted segment. The constriction remained localized in its original segment of gut. Relaxation was occurring in the cecum.

120″ the cecum was again in the process of contraction and a ring-like band was forming in another segment of small intestine which did not move down the gut.

180″ all motility had ceased.

10:50 A.M. The intestines were quiet.

11:05 A.M. The left vagus nerve was exposed in the neck.

11:15 A.M. The left vagus nerve was stimulated with the coil at 10 cm. The heart ceased 1 to 2 seconds, resumed beating, attained a rate of 60 and while still being stimulated resumed its usual rate. The pyloric region of the stomach contracted, but no peristalsis or segmental contractions occurred in the intestines.

11:18 A.M. Spontaneously, a bud was seen forming on the cecum. When the vagus nerve was stimulated, the cecum relaxed. When the stimulus was removed the cecum again contracted.

11:22 A.M. Spontaneously, a bud appeared on the cecum and a ring-like band of contraction was seen forming in the small intestine. With the coil at 10 cm., Point 6 was stimulated. This was followed by acceleration in the movement in both cecum and small intestine.

11:45 A.M. The right cerebral hemisphere was exposed. At this time there was neither peristalsis nor other signs of activity in the gut. Short faradic stimuli applied to Point 5 and other points on the motor area of the right hemisphere excited normal responses in the extremities, but no effect on the intestines.

11:50 A.M. Point 7 on the right hemisphere was stimulated 1 minute with the coil at 11 cm.

30″ after stimulation was started the tip of the cecum was evaginated and a narrow ring-like band circumscribed the small intestine, which was not transmitted.

11:55 A.M. Point 7 was again stimulated with similar results.

12:00 Noon. With the coil at 11 cm., Point 6 was stimulated 1 minute. Activity was observed in the cecum after 50″ but none in the small intestine.

12:05 P.M. Point 1 was stimulated 2 minutes with the coil at 11 cm.

20″ after application of the electrode, the lower end of the cecum contracted vigorously.

30″ a strong ring-like band of contraction appeared in the small intestine, but was not transmitted.

60″ the cecum was beginning to relax.

90″ the cecum had relaxed, but the ring of contraction was still present in the small intestine.

12:10 P.M. Point 3 was again faradized with similar responses to those elicited at 12:05 P.M.

12:24 P.M. 0.4 cc. of ephedrine was given intramuscularly.

12:29 P.M. The heart sounds were strong and rate unchanged. The intestines appeared somewhat dilated and flabby, and slightly paler.

12:30 P.M. The intestines and brain were definitely paler than before. With the coil at 10 cm., Point 1 was stimulated 1 minute. Within a few seconds of the beginning of stimulation, the lower part of the cecum was contracting vigorously. A narrow ring of constriction appeared in the small intestine. The ring circumscribing the intestine widened into a band. It reached 10 mm., then 15 mm. It was not transmitted. Peristaltic waves arising in cephalad segments broke against the contracted segment, but were unable to pass or to alter the band of contraction. One peristaltic wave more forceful than the rest reached the ring of contraction, and simultaneously invagination of the active portion of the gut into the passive segment lying in continuity with it occurred. An intussusception was present which measured 15 mm. in length.

12:36 P.M. The intussusception was still present and unaltered in appearance.

Stimulation of the cerebral cortex, particularly area 6 (Fig. 2), excited activity of an abnormal type in the small intestine. A ring of contraction developed in a segment of bowel and for some reason was not transmitted. Its per-

sistence at one point, aided by peristaltic waves from cephalad segments resulted in invagination of the active portion into the lumen of the passive segment lying in continuity with it. The invagination of the advancing bowel resulted in stimulation of the receiving portion which grasped the entering segment. The administration of adrenalin intramuscularly did not interfere with the effects of cortical stimulation. After the intussusception had persisted 10 minutes, the abdomen was closed and dial was given intraperitoneally. When examined 2 hours later the intussusception had disappeared.

No less striking in this experiment was the rhythmic activity excited in the cecum by cortical stimulation. After activity had been initiated the tip of the cecum often continued to contract and relax for several minutes after stimulation had ceased.

Short stimuli such as give good motor responses of the digits (2-5 seconds) did not excite movements of the intestine. When a 1 minute stimulus was applied, usually 15 to 30 seconds elapsed after stimulation was begun before activity was noted in the intestines. Working against a static background, no inhibitory effects of cortical stimulation were observed.

A detailed protocol of each experiment would require excessive space. However, it would appear advisable to give a summary of each experiment in which the cortex was stimulated because many differences are presented which will be referred to in the discussion.

Experiment 2 (Intussusception IX. Area 6, Series XXV). Immature female Macaca mulatta. Weight 1700 gm. Excitation of activity in cecum and small intestine by stimulation of area 6. Using bipolar electrode under ether anesthesia.

Previous operations. There was a paralysis of the left lower extremity and a sensory level in the left mid-thoracic region as a result of a left hemisection of the spinal cord made at 10:00 A.M. March 24, 1933.

Observations upon intestine—March 24, 1933. Under ether anesthesia the right motor and premotor areas were exposed and the abdomen was opened. Most of the small intestine was atonic and collapsed, and the large intestine was filled with gas. Blood vessels in the intestinal walls were prominent. No intestinal motility was observed.

Faradic stimulation of the motor and premotor areas 5 to 10 seconds caused the usual responses in the extremities. This was repeated several times but no changes in the appearance or motility of the intestines were observed.

Stimuli lasting 2 to 4 minutes applied to the premotor area (Points 1 and 2; Fig. 1) initiated great activity in the cecum and small intestine. Rhythmic contractions of the tip of the cecum were set up at the rate of 2 or 3 a minute, often continuing after the stimulus was removed. A ring-like band of contraction in the small intestine was often produced. Usually a narrow band of contraction appeared, relaxed, contracted again, but was not transmitted. Occasionally during stimulation, a peristaltic wave was seen in the small intestine passing caudally 2 to 3 cm., then in the opposite direction in the same piece of gut.

The latent period from the application of the stimulus to the appearance of intestinal activity, was usually as great as 60 seconds during the first part of the experiment, and often as little as 10 seconds during the latter part.

Stimulation of Point 2 produced the greatest activity. Often no increase in motility was obtained from nearby points.

Experiment 3 (Area 6, Series XXII. Intussusception X). Immature male Macaca mulatta. Weight 2300 gm. Production of peristalsis and a transient intussusception in the small intestine, and a "peristaltic rush" in the large intestine by stimulation of area 6.

Previous treatment. Food was withheld from the animal four days and phloridzin injected daily for an experiment in carbohydrate metabolism. At the beginning of the metabolism experiment the animal was normal except for a diarrhea which had been present several days.

Observations upon intestine—March 29, 1933. Under ether anesthesia the left cerebral cortex was exposed and the abdominal cavity opened. The liver presented a typically diabetic appearance. The small intestine was completely collapsed with the walls in contact and longitudinal striations plainly visible. The transverse colon had a beaded appearance, but there were no bands of constriction. No activity was observed in the gastrointestinal tract. The intestines were floated in a bath of normal saline at 38° C. Within a few seconds peristalsis appeared in many loops of small intestine, but ceased in 5 minutes.

Stimulation of Point 1 (Fig. 2) with a bipolar electrode excited ring-like bands of contraction in the small intestine which were not transmitted. After this point had been stimulated faradically several times for 1 minute each, an intussusception made its appearance. Ten minutes after it was first observed, the intussusception spontaneously released itself.

One minute faradic stimulation of Point 4 initiated a vigorous "peristaltic rush" in the descending colon. The wave of contraction began 15 seconds after the application of the electrode. This was transmitted rapidly through 16 to 18 cm., the colon contracting down like a cord and straightening out like a coiled rubber tube when a stream of water is passed

through it. The activity lasted 2 minutes after the stimulus ceased and gradually relaxed. Point 4 was stimulated 6 different times, each time causing a striking "peristaltic rush". When the electrodes were moved a few mm. distant from Point 4, stimulation failed to excite peristalsis.

Once during the experiment, the anesthesia became too light. When ether was administered, the animal struggled and a "peristaltic rush" occurred in the large intestine similar to that produced by stimulation.

Experiment 4 (Bouton V. Intussusception XII). Immature female Macaca mulatta. Weight 2000 gm. Rhythmic contractions of the cecum initiated by faradic stimulation of area 6.

Previous operations. March 27, 1933, the left premotor area was extirpated with a resulting right hemiparesis.

Observations upon intestines—March 30, 1933. The right motor and premotor areas were exposed and the abdomen was opened under ether anesthesia. The small intestine was collapsed. The large intestine contained a small amount of gas and fecal material. No peristaltic activity was visible in the intestines. The animal was placed in a bath of normal saline at 38° C. so that the intestines were partly submerged and partly floating. The change in environment did not result in increased motility of the intestines.

Stimulation of Point 4 faradically with a bipolar electrode 1 minute elicited contraction of the cecum. After a latent period of 30 seconds a bud-like process appeared on the end of the cecum. When Point 4 was stimulated 6 minutes later, the latent period was only 15 seconds and rhythmic contractions were set up at the rate of 1 cycle per minute, i.e., contraction occurred producing a bud and relaxation followed within a minute. Similar activity in the cecum was elicited by stimulation of Point 3 (Fig. 2).

At no time was motility observed in the small intestine or colon. No response could be obtained in the cecum 20 minutes after the first cortical stimulation. Likewise, stimulation of the motor area with twice the usual strength failed to yield movement of the extremities at this time.

Experiments 2, 3 and 4 confirm the results given in detail in Experiment 1. Stimulation of area 6 excited rhythmic activity in the cecum of all 3 animals. In Experiments 2 and 3, ring-like bands of contraction which were not transmitted appeared in the small intestine under the influence of premotor stimulation. In Experiment 3 a transient intussusception was observed, and a "peristaltic rush" was produced in the large intestine.

It was observed that the responses of the gastrointestinal tract to cortical and vagus stimulation were dissimilar. When the vagus nerve was stimulated in the neck, contraction of the pyloric region of the stomach occurred, followed by contraction of the body of the stomach. When the cortex was stimulated, the stomach did not appear to be affected, but definite activity resulted in the intestines. The observations suggested selected action on specific fibers or that some pathway other than the vagus might contain motor fibers to the gastrointestinal tract. As one method of attacking the problem several animals were vagotomized and the cortex stimulated. The following experiments (5, 6, and 7) show the results as well as some of the difficulties of interpretation.

Experiment 5 (Hypothalamus VIII. Intussusception XVI). Mature male Macaca mulatta. Weight 6300 gm. Activity of cecum and small intestine elicited by faradic stimulation of the premotor area. Slight motility excited in small intestine by cortical stimulation after bilateral vagotomy.

Previous operation. A small lesion was made in the hypothalamus by the transcallosal route. Except for a rapid gain in weight following operation, the animal was normal in every respect.

Observations upon intestines—June 9, 1933. The experiment was performed under ether anesthesia. A right osteoplastic flap was elevated and both vagus nerves were exposed in the neck. Immediately after the peritoneal cavity was opened the animal was placed in a bath of normal saline at 38° C. The small intestine contained a little gas, but most of the intestine lay with the walls in contact; the cecum was relaxed, but the colon was constricted. No peristalsis or segmentation was seen. A spontaneous contraction of the cecum was observed before electrical stimulation was begun. A definite bud-like evagination appeared and relaxed.

Faradic stimulation of Point 1 (Fig. 2) initiated vigorous rhythmic contractions of the cecum associated with mild peristaltic movements of the small intestine. Activity in the cecum continued 3 minutes after the stimulus ceased. On one occasion during the experiment the depth of anesthesia became very light. When ether was administered the animal struggled, and during the struggles vigorous motility in the cecum of a rhythmic character appeared.

Cutting the left vagus nerve in the neck appeared to cause pain, and the cecum contracted strongly. While the cecum was in a state of moderate contraction the left vagus nerve was sectioned. Relaxation and dilatation of the cecum and colon appeared immediately, but no change was noted in the small intestine. Considerable respiratory difficulty ensued.

Point 1, stimulation of which excited activ-

ity in the cecum and small intestine before vagotomy, was again stimulated faradically. After a latent period of 30 seconds, a ring-like band of contraction made its appearance in the small intestine. Five minutes later, Point 1 was again stimulated, and this time after 90 seconds' stimulation, a similar band of contraction appeared in the small intestine. The cecum responded in no way.

The animal died a respiratory death. No peristalsis or segmentation was present during the respiratory difficulties just preceding death. However, 2 minutes after the pulse and respiration ceased, vigorous activity began in the cecum, and active peristalsis and forceful rhythmic segmentation were observed in the small intestine. This extreme activity lasted 3 to 4 minutes and then ceased rather abruptly.

Experiment 6 (Pilocarpine XIII. Intussusception XIV). Immature female Cercopithecus sabaeus. Weight 2500 gm. Initiation of peristaltic activity by stimulation of area 6 after bilateral vagotomy.

Previous operations. December 8, 1932, a complete subdiaphragmatic vagotomy was done on the left side. February 17, 1933, the right vagus nerve was sectioned in the neck, sparing the laryngeal branch.

Observations upon intestines—March 28, 1933. Both motor and both premotor areas were exposed using ether anesthesia. The left vagus nerve was dissected free in the neck. Both cut ends of the previously sectioned right vagus were identified. The distal end of the right vagus was adherent to the recurrent laryngeal nerve.

The animal was placed in a bath of normal saline at 38° C. when the peritoneal cavity was opened. The small intestines were distended with gas. Several slowly contracting isolated bands were noted and one peristaltic wave was seen moving down the gut. The cecum was dilated and the colon was constricted; both were quiet.

Stimulation of Point 1 and Point 2 of the right hemisphere excited no response in the gastrointestinal tract. When the peripheral stump of the right vagus nerve was stimulated it produced definite activity in the small intestine. One minute stimulation of Point 1 of the left hemisphere caused ring-like bands of contraction in the small intestine within 15 seconds after the application of the electrodes. The segmental contractions were maintained 3 or 4 minutes. After section of the left vagus nerve faradization of the peripheral end produced the characteristic cardiac and respiratory responses, but no effect on the gastrointestinal tract.

After carefully destroying all nerve fibers in and near the carotid sheath on both sides of the neck including any part of the vagi that might possibly have been left behind, Point 1 on area 6 of the left hemisphere was again stimulated. Again intestinal activity was increased, though the response was definitely less than those obtained in the early part of the experiment.

Experiment 7 (Intussusception II. Pilocarpine XVIII). Immature female Macaca mulatta. Weight 1700 gm. After previous complete subdiaphragmatic vagotomy, no response of intestinal tract followed cortical stimulation.

Previous operations. On *February 17, 1933,* a complete bilateral subdiaphragmatic vagotomy was performed.

Observations upon intestines—March 7, 1933. Under ether anesthesia the left cerebral cortex was exposed. When the peritoneal cavity was opened, considerable activity was present in the gastrointestinal tract. A ring-like band of contraction 3-4 mm. wide was being transmitted down the small intestine at the rate of a normal peristaltic wave. The band of contraction was sharply delimited and very pale due to the fact that blood was being forced out by the tightly contracted intestinal musculature. In addition, the usual type of peristaltic waves was observed in the small intestine. The cecum was undergoing rhythmic contractions. In the systolic phase, the evagination formed on the end of the cecum resembled a vermiform appendix. This type of activity continued uninterrupted during the 20 minutes of observation.

With the unipolar electrode and the indifferent electrode in the rectum, various points on the cortex were stimulated. Normal motor responses of the arm and leg were obtained from areas 4 and 6 (Fig. 2). However, no effect was observed on motility of the intestinal tract even when the strength and duration of cortical stimulation were more than doubled. The intestinal movements were neither accelerated nor inhibited from any part of the cortex.

After first stimulating the premotor area and obtaining good responses in the intestinal tract, a bilateral vagotomy was done in the neck. Following vagotomy, cortical stimulation appeared to cause an increase in motility, though definitely less than before vagotomy (Experiments 5 and 6). The latent period was unusually long before the response was noted. One naturally asks if all the vagus fibers in both sides of the neck were destroyed. It is believed that all fibers in both sides of the neck were destroyed. In one case Bechterew and Mislawski[6, 7] observed contraction of the small intestine on stimulating the last two thoracic and the first lumbar nerves.

However, cortical stimulation in one animal (Experiment 7), which previously had a complete bilateral subdiaphragmatic vagotomy, failed to elicit responses in the intestines. One

animal (protocol not presented) with generalized peritonitis failed to give the usual intestinal response on cortical stimulation. Using dial as an anesthetic, cortical stimulation failed to excite intestinal activity. This is well demonstrated in Experiment 8 and confirmed by the use of dial in the latter part of Experiment 10. Whether or not it has any significance here, it may be noted that Bucy[9] was unable to elicit movements of the ipsilateral extremities under this anesthetic, though he could obtain them under ether.

Experiment 8 (Intussusception III). Medium sized Macaca mulatta. Weight 2250 gm. Under dial anesthesia, cortical stimulation had no influence on intestinal motility.

Previous operations. March 8, 1933, under dial anesthesia, Dr. Paul C. Bucy, who was studying the effects of cortical stimulation on ipsilateral movements of the extremities, had repeatedly stimulated area 6. No movements of the ipsilateral extremities could be elicited, but the contralateral extremities responded essentially as under ether anesthesia.

Observations upon intestines—March 8, 1933. The peritoneal cavity was opened at the conclusion of the experiment noted above. The stage of anesthesia was very light. The small and large intestines were atonic or relaxed, and the blood vessels were injected. No peristalsis was observed.

Points 1, 2, 3, 4 and others were stimulated with a bipolar electrode, gradually increasing the strength to well above that usually employed. No response was seen in the intestines and their appearance was not altered.

Application of the electrode to the peritoneal surface of the small intestine excited a ring-like band of contraction at the site of the stimulus. The contraction appeared after 5 to 10 seconds of stimulation and was not transmitted.

Stimulation of the left vagus nerve in the neck 15 seconds gave the usual cardiac response and a vigorous contraction of the pyloric region of the stomach, but no alteration in the intestines. When the nerve was stimulated 45 seconds similar results occurred and in addition very gentle intestinal peristalsis.

In most of our earlier experiments, the chief aim was to determine whether or not cortical stimulation had any influence on gastrointestinal motility. Since the autopsies suggested a relationship with area 6, this region was usually chosen first for stimulation. After this fact had been established, other areas within the operative field were stimulated. Experiments 9 and 10 demonstrate that intestinal motility can be produced by faradic stimulation of the postcentral gyrus and the frontal region anterior to area 6. Attention is called to the fact that stimulation of the postcentral gyrus within 1 or 2 mm. of the central sulcus excited intestinal activity, but did not excite movements in the extremities such as would have been the case had there been a spread of current. Also as control, after stimulating a point on the cortex, the electrode was transferred to the falx cerebri adjacent to it. When there was any indication of a spread of current, the strength of the current was reduced and new observations made. Experiment 10 is considered significant as suggesting a possible influence of the frontal and postcentral areas upon intestinal movements, because area 6 had been ablated at a previous operation.

Experiment 9 (Corpus callosum IX. Intussusception XV). Immature Macaca mulatta. Weight 2800 gm. Motility of cecum initiated by faradic stimulation of the premotor area and the postcentral gyrus.

Previous operations—On *May 19, 1932,* a left bone flap was elevated, the anterior cerebral artery ligated at the genu of the corpus callosum, and the corpus callosum sectioned. Three days later after stimulation of areas 4 and 6 on the right side these were extirpated. The animal's condition remained good, and during the following week it recovered considerable use of the left arm and leg so that locomotion was quite good.

Observations upon intestines—May 31, 1933. Under ether anesthesia, the left bone flap was reëlevated and the abdomen opened. No motility was observed in the small intestine or the colon. The cecum was seen to contract slowly once over a period of five minutes. The intestines were floated in normal saline 38° C. without excitation of motility.

Faradic stimulation of Point 1 (Fig. 2) with a bipolar electrode for one minute initiated a vigorous contraction of the cecum. The contraction started 20 seconds after the electrode was applied to the cortex. Rhythmic contractions of the cecum continued after the stimulus ceased, a cycle of contraction and relaxation lasting about one minute.

Likewise stimulation of Point 7 on the postcentral gyrus excited rhythmic contractions of the cecum. Spread of current was excluded by applying the electrode to the falx cerebri near Points 1 and 7 without effect.

No motility was observed in the small intestine or the colon. No further responses could be obtained in the cecum 20 minutes after the first cortical stimulus. However, faradic stimulation of the left vagus nerve was still effective, causing slowing of the heart, contraction of the pyloric region of the stomach, but no effect on the intestines. A second vagal stimulus appeared to excite activity in the cecum; and a

third appeared to inhibit it, i.e., no effect was noted as long as the electrodes were on the nerve, but motility began as soon as they were removed.

Experiment 10 (Intussusception XVII). June 27, 1933. Macaca mulatta. Weight 2000 gm. After previous extirpation of area 6, faradic stimulation of postcentral gyrus and frontal region excited intestinal activity.

Previous operations—January 11, 1933, area 4 was excised from the left hemisphere.

February 6, 1933, through a right bone flap area 6 was ablated.

Observations upon intestines. The right bone flap was reëlevated under ether anesthesia and the peritoneal cavity opened. The animal was placed in normal saline at 38° C. partly submerging the intestines. The stomach was small. Little material was present in the small intestine and the walls were often in contact with each other. Neither peristalsis nor rings of contraction were observed.

Stimulation of the crater at the site of ablation of the premotor area produced no responses in the extremities or the intestines. However, faradic stimulation with the bipolar electrode of Point 7 (Fig. 2) on the postcentral gyrus and Point 8 in the frontal region excited definite responses. Peristalsis involving one or two segments and occasionally a "peristaltic rush" was produced by stimulating these areas. No ring-like bands of contraction were observed.

Stimulation of area 4 caused the usual motor responses in the extremities, but none in the gut.

Several times when the depth of anesthesia became light and ether was administered, the intestine was seen to relax or become atonic. Peristalsis was never excited by the administration of ether, as in some other experiments, but in this one no remarks were made on the presence or absence of an excitement stage.

After the preceding observations had been completed, dial was given intraperitoneally. Two hours later, the small intestine was uniform in calibre; there were no constricting rings. Mild peristalsis was seen in several segments of small intestine for 2 or 3 minutes after the abdomen was reopened. At this time, stimulation of the frontal and postcentral gyri, with the same duration and strength of stimulus, failed to excite any response in the intestines. Stronger stimuli were also ineffective.

In the following experiments area 6 was stimulated two and one-third seconds per minute for two and a half to three hours and movements of the extremities observed. The abdomen was not opened until the stimulation experiment ended. In all three animals the gastrointestinal tract presented signs of excessive activity and all had intussusceptions of recent occurrence. As far as the gastrointestinal tract is concerned, the conditions were physiological, as the peritoneal cavity was not opened. Another point illustrated is that repeated short faradic stimuli are effective in exciting activity in the intestine.

Experiment 11 (Area 6 III). Macaca mulatta. Weight 1450 gm. Repeated brief stimulation of premotor area. Autopsy: four recent intussusceptions in ileum.

Previous experiments.—On *January 12, 1933,* the left motor area had been removed, and on February 23, both cerebral hemispheres were exposed and stimulated faradically. No motor responses could be obtained from the left hemisphere, but the right hemisphere yielded vigorous motor responses which were studied over a period of three hours during which stimuli were applied intermittently to the motor and premotor area.

Autopsy (February 23, 1933). The animal was sacrificed soon after the previous experiment. When the peritoneal cavity was opened, four separate and distinct intussusceptions were disclosed in the lower ileum, the first about 18 inches below the pyloric sphincter, and the fourth, which was an inch in length, was 5 inches from the ileocecal valve. The blood supply to the ileum appeared normal, and all four intussusceptions were clearly recent. The small intestines also showed intermittent rings of spastic contraction, similar to those described in the preceding experiments.

Experiment 12 (Intussusception VII. Area 6 XVI). March 7, 1933. Immature Macaca mulatta. Weight not determined. Repeated short stimuli to area 6 with abdomen intact. Intussusception at autopsy.

Previous experiment—March 7, 1933, under ether anesthesia area 6 was stimulated two and a third seconds per minute for 3 hours by workers who were studying the relation of this area to movements of the extremities.

Autopsy. When the animal was sacrificed immediately after the preceding experiment, an intussusception one and one half cm. long was found in the ileum 41 cm. below the pylorus. There was no disturbance of blood supply. Eight cm. caudally a constricted segment of gut was beginning to enter the relaxed segment in continuity with it, a fold having formed along the periphery opposite the mesentery.

The pyloric region of the stomach was markedly contracted and the body measured only three and one-half cm. in diameter. The mucosa was thrown into high folds.

Experiment 13 (Area 6 XV). March 4, 1933. Immature Macaca mulatta. Weight not determined. Faradic stimulation of area 6 of short duration repeated. Intussusception disclosed on opening abdomen.

Previous experiment—March 3, 1933. For the purpose of making observations on the extremities, the premotor area was stimulated two and one-third seconds per minute for two and one-

half to three hours. The abdomen was untouched.

Autopsy. On sacrificing the animal and opening the peritoneal cavity an intussusception one and one-half cm. long was disclosed 30 cm. below the pylorus. There was no evidence of a disturbance of blood supply to the intestine.

The pyloric sphincter and antrum were greatly contracted and were very firm on palpation. The fundus and cardiac portions of the stomach were more dilated. When the stomach was opened, it was seen to be filled with thick mucoid material which could not be washed off with a stream of water. The crests of the mucosal folds were speckled with punctate hemorrhages. The intestine proximal to the intussusception was filled with the whitish, glairy, mucoid secretion from the stomach.

IV Discussion

In the preceding experiments it has been shown that faradic stimulation of the premotor area and certain adjacent parts of the cerebral cortex of monkeys excites the intestines to vigorous motor activity. It seemed difficult, however, to harmonize this fact with the occurrence of intussusceptions following the removal of the premotor and adjoining areas of cortex. A possible solution to the paradox has come from a survey of relevant literature which has indicated that the gut representation in the cortex includes both excitatory and inhibitory units. Cortical ablations appear to cause enhancement of motor activity through the release from the inhibitory components and through a generalized disturbance of the delicate balance normally existing between these mutually antagonistic elements.

1. *Faradic stimulation.* The earliest reference to the effects of cortical stimulation on intestinal motility which could be found was by Bochefontaine[8] in 1876. He demonstrated that stimulation in the region of the sigmoid gyrus of the dog usually diminished or even completely stopped rhythmic contractions of the stomach. However, the inhibition was often immediately preceded by a strong peristaltic contraction of the entire pyloric region. Movements of the small and large intestines were also found to occur under the influence of cortical stimulation. Peristalsis appeared in different parts of the small intestines in varying intensities; sometimes the duodenum was active, at others, the ileum. Many times peristalsis of the large intestine was so forceful that it carried the fecal contents ahead of it. Exceptionally, cortical stimulation yielded no appreciable results.

Hlasko[18] observed that stimulation of the cortex in the region of the cruciate sulcus in the dog caused inhibition of the cardiac sphincter. He obtained contraction of the cardia and the wall of the stomach by stimulating the corpora quadrigemina. Openchowski[31] localized an area close to the cruciate sulcus from which he elicited opening of the cardia and closing of the pylorus. Like Hlasko, he produced similar changes by stimulating the corpora quadrigemina, and also by stimulating the corpus striatum and the lenticular nucleus. Bechterew and Mislawski[6, 7] by faradic stimulation of the sigmoid gyrus and the area posterior, were able to change the condition of the intestinal musculature. Occasionally the occipital region gave similar results, but stimulation of other areas was entirely without effect. The usual effects were an alteration in tonus and an increase in peristaltic activity in a few loops of intestine. Stimulation excited contraction and relaxation of the small intestine followed by similar movements in the large intestine.

Osipov[32] isolated two points on the sigmoid gyrus anterior to the cruciate sulcus, one at the outer margin of the sulcus and the other close to the inner margin of the hemisphere. From these points he excited contraction of the large intestine. In some animals stimulation was effective at the outer point, in other animals at the inner point, but not from both, and nothing could be obtained from the surrounding cortical tissue. von Pfungen[36] observed an increase in peristalsis on stimulating the sigmoid gyrus and its surroundings. Often, however, from the same cortical area, stimulation inhibited peristaltic movements.

It appears, then, that stimulation of certain points in and around the sigmoid gyrus results in increased peristalsis; from other points in this region peristalsis is inhibited, and stimulation of still other points has no noticeable influence on gastrointestinal motility.

The results of other authors are in complete accordance with our observations. Cortical stimulation in our experience sometimes produced peristalsis in the small intestine, and at others ring-like bands of contraction which were not transmitted. In some animals activity could be obtained only in the large intestines. Usually intestinal motility could be influenced from most of the premotor area, often from the prefrontal region and occasionally from the postcentral gyrus. Yet not every point within this circumscribed area on stimulation gave increased peristalsis. Inhibition of peristalsis such as was obtained by other experimenters from cortical stimulation was not observed, but this may be due to the fact that there was little peristalsis in the monkey under the conditions of the experiments. In one animal, from which such striking "peristaltic rushes" in the large intestine were initiated, stimulation was effective only from the anterior margin of the superior precentral sulcus.

2. *Ablation and release of function.* What effects on the gastrointestinal motility have been noted following removal of the influence of the cerebral cortex or certain parts of it?

Ott and Field[33] observed that quiet peristalsis in the cat became very active after the brain was sectioned posterior to the thalami. Similar observations were made by Bechterew[5]. He often noted that defecation occurred soon after the section was made. In decerebrate, vagotomized cats with the intestines floated in normal saline, Lurje[26] noted spontaneous contractions of the large intestine over a distance of 5 or 6 cm. The contraction was often of such intensity that the intestine was contracted down like a cord, snow-white due to squeezing out all of the blood. After beginning, the activity often lasted 20 minutes or more. Since the vagus nerve does not innervate the large intestines, certainly not the transverse and descending colons, the results may be considered in the light of the section of the brain.

Pal and Berggrün[34] approached the problem in another manner. They stimulated the right vagus nerve 15 seconds and excited contraction of the pyloric region of the stomach, but no movement of the small intestine. Stimulation of the left vagus gave a similar result. Then they made a section through the medulla and stimulated again.

11:02 Complete section of the medulla oblongata.
11:10 Stimulation of R. vagus 10 seconds—with contraction of the stomach there was also a slight contraction of the small intestine.
11:12 Stimulation of L. vagus 10 seconds—definite intestinal peristalsis.
11:16 Stimulation of R. vagus 10 seconds—active intestinal peristalsis.
11:35 Stimulation of L. vagus 10 seconds—vigorous intestinal peristalsis.
11:48 Stimulation of R. vagus 10 seconds—definite intestinal peristalsis.

The table giving the time and result of vagus stimulation makes it evident that the most marked activity appeared 14 and 33 minutes after the operative procedure. This point will be referred to later.

In subsequent experiments Pal and Berggrün[34] made more cephalad sections of the brain, stimulating the vagus nerves before and after the section, and observing the effect on intestinal peristalsis. In a series of dogs they made sections of the brain stem in the middle of the thalami; in another series they made sections anterior to the thalamus immediately behind the head of the caudate nucleus; and finally in one group they extirpated both sigmoid gyri. In every group, vagal stimulation had little effect on intestinal motility before section of the brain, and in every group after section of the brain, vagal stimulation excited lively peristalsis in the small intestine. Often when first observed the intestines were narrow and pale or cyanotic. Following section of the brain the intestines appeared relaxed and redder in color.

One would conclude from the observations of Ott and Field[33], Bechterew[5], Lurje[26], Pal and Berggrün[34] and our own extirpation experiments that certain parts of the cerebral cortex, i.e., sigmoid gyrus and its neighborhood in the dog and cat, and the premotor area and its neighborhood in the monkey, normally exert an inhibitory influence upon intestinal motility. When the influence of the cortex is removed by extirpation, a release of function occurs, allowing excessive and perhaps abnormal intestinal motility.

Release of function raises the question of irritation. The observation of Bechterew[5] that defecation occurred soon after the brain stem was sectioned behind the thalamus, might be accounted for on the basis of irritation. It is very unlikely, however, that irritation from the section played any part in exciting intestinal peristalsis in the vagus stimulation experiments of Pal and Berggrün 33 minutes after the operative procedure. Sherrington's work on decerebrate rigidity[39] and spinal transection indicates, moreover, that irritation from a transection of cord or cerebral substance rarely lasts for more than 10 minutes. Ruch and Watts[38], in demonstrating the release of function in the forelimb extensor muscles following postbrachial spinal transection, find that similar signs of irritation disappear within 10 minutes after the lesions were made. Evidences of irritation after injury to peripheral nerves may be somewhat more prolonged, but not longer than an hour[1].

3. *Intussusception from local stimulation.* Nothnagel[28] has shown that by placing a crystal of sodium chloride on the peritoneal surface of the intestine contraction occurs above the point of irritation, whereas complete rest prevails below. Nothnagel[29] also demonstrated that it is possible to produce artificial invagination of the bowel in living rabbits by the application of faradic current to the intestinal wall. Cannon[12] states that "the modern conception of intestinal peristalsis was, however, not fully stated until Mall[27] pointed out the significance of Nothnagel's observation on intussusception. Nothnagel had reported that the *intussuscipiens* portion of the gut, lying below the point of stimulation, folds back, and extends upward over the contracted *intussusceptum* lying above. Thus contraction above and relaxation below seemed so related as to be parts of a single act. And Mall concluded that while a mass in the intestine is causing contraction above, which forces the mass downward and thus stimulates fresh regions above to contract, active dilatation below is at the same time inviting an easy descent. Peristalsis would thus be another example of the mutual adjustment of antagonistic muscles toward efficient action—an example which presents in the neuromusculature of the gut the important principles . . . named by Sherrington. . . 'reciprocal' innervation".

When the premotor area and adjacent parts of the cerebral cortex are stimulated or excised, this local reciprocal innervation appears to be disturbed. In a group of the animals the resulting imbalance was sufficient to excite the production of an intussusception.

4. *Relation of skeletal movement to gut movements.* Since the induced activity of the intestines in our experiments was usually associated with slow rhythmic movements of the extremities (from premotor stimulation) the question arises whether the increased intestinal movements have any relation to the movements of the skeletal muscle. It seems improbable that contraction of skeletal muscles could be a primary stimulus since faradization of area 4 caused vigorous movements of the contralateral extremities, but was without effect on the intestines. Also, stimulation of the postcentral gyrus and the frontal region anterior to area 4 produced increased motor activity of the intestines but no activity of the extremities.

In several experiments when the depth of anesthesia became light, struggling movements occurred as ether was renewed and this was associated with marked augmentation of intestinal activity similar to that seen in response to stimulation of area 6. As the depth of anesthesia increased, all intestinal movements decreased.

5. *Pathways involved.* The pathways by which impulses travel from the cerebral cortex to the intestinal musculature have not been adequately studied. They are clearly extrapyramidal paths because stimulation of area 4 failed to elicit activity in the intestines. Poliak[37] has shown that there are tracts from the frontal and precentral cortex to the red nucleus and substantia nigra; possibly there are tracts also to the hypothalamus. In the hands of Beattie[2] stimulation of the lateral margin of the infundibulum in cats excited marked increased peristalsis and secretion in the stomach provided barbiturates were not used as anesthetics. (See also Sheehan and Beattie[38a].) The usual effects of hypothalamic stimulation similarly could not be elicited in man under avertin anesthesia (Cushing[14]), and in monkeys under "Dial-Ciba" anesthesia we have been unable to evoke motor responses of the intestine. The failure to obtain responses in animals anesthetized with barbituric acid derivatives is probably attributable to the site of action of the anesthetic, for E. and J. Keeser[20] have shown that the majority of barbituric acid derivatives act primarily upon the hypothalamic and thalamic nuclei.

Although the results in our experiments of cortical stimulation after vagotomy do not admit a definite interpretation it would appear that most excitor impulses to the small intestine reach it through the vagus, but some also may reach the small intestine by way of the spinal cord and then by preganglionic fibers of the sympathetic system. Intussusception was never produced in vagotomized animals nor were we able to detect alteration of gastric secretion in such animals.

The clinical implications of these studies, particularly in reference to morbid hunger and the gastrointestinal manifestations of focal and generalized epilepsy will be deferred to a future communication.

Summary

The relation of the cerebral cortex to the motility of the gastrointestinal tract has been studied in a series of monkeys (*Macaca mulatta*) which, prior to stimulation of the cortex, had had lesions made in various parts of the cerebral hemispheres. The gastrointestinal tracts of 65 unstimulated or unoperated monkeys were carefully studied as controls. The chief observations and conclusions are as follows:

1. Intussusception with fatal obstruction occurred spontaneously in three healthy monkeys in which the region of the premotor area (area 6) of the cortex had been removed from both hemispheres. Prior to this experience spontaneous intussusception has been encountered only twice in the course of 300 autopsies on monkeys carried out in the laboratory during the past three years, in both instances in acutely ill unoperated monkeys (probably agonal).

2. Carefully controlled faradic stimulation of the monkey's cortex in the premotor region gives rise to active peristaltic movements of the gut, and in 2 experiments with continuous stimulation (1 to 2 minutes) well-marked multiple intussusceptions were produced by this procedure. In three instances stimuli were applied intermittently over a period of several hours (Experiments 11, 12 and 13) and multiple intussusceptions were found on opening the abdomen.

3. Stimulation, brief and prolonged, of the motor area (area 4), which gives rise to vigorous movements of the skeletal musculature, failed to influence the movements of the gut.

4. Stimulation of the premotor area from certain points relaxed the stomach sphincters.

5. Intussusception could never be obtained after the vagi had been sectioned, but stimulation of the premotor region in such preparations occasionally caused slight increase in peristaltic movements (the influence of the integrity of the sympathetic pathways was not studied).

6. In some experiments cortical stimulation caused increased secretions of the gastric juice.

7. In one instance (Experiment 10) stimulation of the frontal and postcentral convolution in a monkey from which the premotor area had been removed 5 months before caused increase in peristaltic movements, but not intussusception.

8. It is concluded that the cerebral cortex of monkeys contains autonomic representation for the gastrointestinal tract which is largely restricted anatomically to the premotor area, and that this representation includes both excitatory and inhibitory components.

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OBSERVATIONS ON THE CHEMICAL AND PHYSICAL RELATION BETWEEN BLOOD SERUM AND BODY FLUIDS*

II. The Chemical Relation Between Serum and Edema Fluids As Compared With That Between Serum and Cerebrospinal Fluid

BY D. ROURKE GILLIGAN, M.S.,‡ MARIE C. VOLK, A.B.,‡ AND HERRMAN L. BLUMGART, M.D.‡

WHETHER cerebrospinal fluid is a dialysate in equilibrium with blood plasma has been the subject of many investigations since 1912, when Mestrezat[1] first introduced this theory. It is generally held by the proponents of the dialysate† theory of cerebrospinal fluid that the chemical composition of such fluid, so far as the major constituents are concerned, is that which would be expected from a simple membrane equilibrium. It seemed that a comparison of the distribution of substances between serum and edema fluids, which we have shown to be simple dialysates in a previous communication[2], with the reported distribution of substances between serum and cerebrospinal fluid would offer

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†In the literature the term dialysate has been used interchangeably with the term ultrafiltrate in reference to cerebrospinal fluid. The term dialysate has been employed in this communication to comply with the most current usage. The assumption is made that the composition of a plasma ultrafiltrate formed under physiological conditions would be the same, or approach closely, that of a dialysate at equilibrium (Greenberg, D. M., and Greenberg, M.: J. Biol. Chem., 94:373, 1931).

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a basis for testing the validity of the dialysate theory of cerebrospinal fluid.

The approximate equality of osmotic pressure as measured by the freezing point of depression of serum and normal cerebrospinal fluid[3] is in harmony with the dialysate theory. Since the osmotic pressures of secretions, such as gastric juice[4] and hepatic bile[5], are likewise approximately equal to the osmotic pressure of serum, the proof of the dialysate nature of cerebrospinal fluid must rest on the conformity of the distribution of the individual substances between serum and cerebrospinal fluid to the distribution demanded by the physicochemical laws of dialysates.

The chemical complexity of the serum does not allow an abstract definition of the true chemical state of all of its constituents. Thus, a measure of the total concentration of a given constituent of the plasma may not necessarily represent the amount which will be distributed across a semi-permeable membrane, in accordance with the Donnan law of equilibrium. For example, it is well known that the calcium of the plasma consists of both diffusible and non-diffusible forms. The distribution of the total calcium between serum and its dialysates, therefore, cannot be interpreted in terms of equilibrium laws alone.

Dialysis experiments between blood plasma and body fluids performed "in vitro" with artificial membranes are open to the criticism that physiological conditions are not reproduced. The proof of the dialysate nature of cerebrospinal fluid must then be based on the conformity of the distribution of substances between serum and cerebrospinal fluid with the distribution of the same substances between serum and other body fluids which can safely be considered dialysates on both a physiological and a physicochemical basis.

The data obtained in this laboratory[2] and the results of other investigators[6, 7, 8, 9, 10] on the distribution of substances between edema fluids and serum leave no doubt that edema fluids from patients with congestive heart failure, nephritis, carcinomatous obstruction and cirrhosis of the liver are simple dialysates in equilibrium with blood plasma.

It must be considered whether the distribution of substances between serum and edema fluids differs fundamentally from the distribution between serum and normal interstitial fluids. The studies of Heim[11] and of Arnold and Mendel[12] on the distribution of certain substances between the serum and lymph of the normal dog indicate that the same laws which characterize the equilibrium between serum and edema fluids also characterize the equilibrium between serum and lymph. When the average values reported by Heim[11] are calculated in terms of the water content of the serum and lymph, the ratios of the concentrations of chloride, calcium, inorganic phosphate and certain non-electrolytes in serum and lymph are closely in accord with the ratios of the concentrations of the same substances in serum and edema fluids with similar concentrations of protein[2]. It is clear, therefore, that edema may be considered as primarily a quantitative rather than a qualitative abnormality.

The possibility that one living body membrane may differ in permeability from another living body membrane must also be considered in this analysis. Further, the composition of ventricular fluid as well as lumbar fluid must be utilized, since the concentration of some substances in the cerebrospinal fluid varies at different levels[13]. Although the protein concentration of normal cerebrospinal fluid is somewhat less than that of even those edema fluids which contain the smallest amounts of protein, comparison of the chemical composition of edema and ceerbrospinal fluid may be made,

TABLE 1

AVERAGE CONCENTRATION RATIOS FOR SUBSTANCES IN SERUM AND EDEMA FLUIDS AND IN SERUM AND CEREBROSPINAL FLUID*

Substance	Ratio†	Ratio for Edema Fluids	Ratio for Cerebrospinal Fluid
Total N. P. N.	Fluid / Serum	0.98	0.6
Creatinine	Fluid / Serum	0.97	0.8
Sugar	Fluid / Serum	1.06	0.6
Chloride	Serum / Fluid	0.98	0.87
Bicarbonate	Serum / Fluid	1.01‡	1.18
Inorganic Phosphate	Serum / Fluid	1.03	2.6
Sodium	Fluid / Serum	0.96	0.96
Calcium	Fluid / Serum	0.70	0.5
	Calculated Donnan Ratio	0.955	0.94

*Average protein concentration of edema fluids—1.4 Gm. per cent. Cerebrospinal fluid protein values average approximately 0.03 per cent.

†Data for edema fluids taken from paper I of this series (Ref. 2). Values for cerebrospinal fluids calculated from data of the sources indicated in the discussion.

‡Venous blood bicarbonate alone considered in order to compare with venous blood used in studies on cerebrospinal fluid. Mean value for ratio representative of blood midway between arterial and venous is 0.96.

since the effect of protein concentration can be estimated from the physicochemical laws of dialysates.

The relative distribution of various substances between cerebrospinal fluid and serum and between edema fluids and serum is discussed under separate headings below. This analysis is based on the extensive data which have been reported by other investigators for the distribution of electrolytes and non-electrolytes between serum and cerebrospinal fluid, on our own data presented previously[2] and on the data of others for the distribution of substances between serum and edema fluids. Table 1 gives a brief summary of data to be discussed.

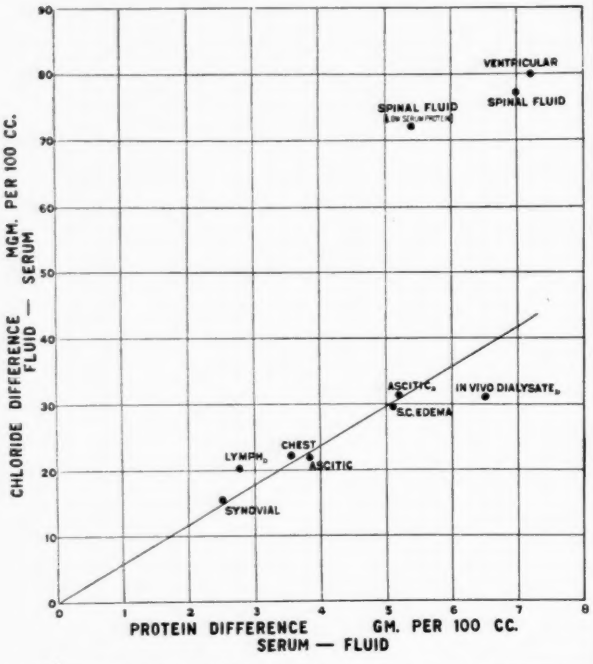

FIGURE 1. The relationship between the average differences in the chloride concentrations of certain body fluids and serum (fluid chloride-serum chloride) and the average differences in protein concentration (serum protein-fluid protein). The values charted represent the average values, in mg. per 100 cc., for the differences in chloride and protein concentration as taken from the literature in the following manner: chest fluid, total of twelve observations from our studies[2], from data of Loeb[9], and from Greene[7]; ascitic fluid, dogs, ten studies by Greene[7]; subcutaneous edema fluid, total of fourteen observations from our studies[2], Gollwitzer-Meier[3], and Hastings[6]; cerebrospinal fluid, total of 29 observations from Fremont-Smith[23] and Hamilton[21]; cerebrospinal fluid with serum proteins averaging 5.5 Gm. per 100 cc., six studies from Fremont-Smith[23]; lateral ventricle fluids, seven studies from Fremont-Smith[23]; "in vivo" dialysates in dogs, fifteen studies from Greene[15]; lymph, dogs, total of seven, six cervical lymph from Heim[11] and one thoracic duct lymph from Arnold[12].

CHLORIDE

According to physicochemical laws the concentration of chloride in a dialysate in equilibrium with serum should be greater than the chloride concentration of the serum. It has been established by many investigators that the chloride concentration of cerebrospinal fluid, whether ventricular or lumbar[13, 14], is considerably higher than that of the serum of the same patient. The chloride concentrations of various edema fluids[2, 6, 7, 8, 9, 10], of lymph[11, 12], of synovial* fluids and of the "in vivo"† dialysates of Greene[15] are also higher than those of the sera.

In figure 1 the average excess of chloride in these fluids as compared with the serum (fluid chloride-serum chloride), has been plotted against the average excess of protein in the serum as compared with the fluids (serum protein-fluid protein). It will be noted that the excess of chloride in edema fluids, lymph, synovial fluids, and the "in vivo" dialysate is proportional to the excess of protein in the serum. In contrast, the excess of chloride in cerebrospinal and ventricular fluids is much greater in relation to the serum protein excess than is the case in the simple dialysates. For example, the edema fluid chloride averages approximately 32 mg. per 100 cc. higher than the serum chloride, whereas the spinal fluid chloride averages 72 mg. higher than the serum chloride when the difference in protein concentrations of the two fluids is 5.4 Gm. per 100 cc. (figure 1).

In one instance measurements were made of the chloride concentrations of serum, subcutaneous edema fluid, chest fluid, ascitic fluid and cerebrospinal fluid from a patient with congestive heart failure who had fasted for fourteen hours (table 2). The chloride was measured by the method of Wilson and Ball[16] and the protein by the method of Dyer[17]. The results obtained in this instance are similar to those found by employing average values as in figure 1. The excess of chloride in the cerebrospinal fluid (table 2) is strikingly higher, in respect to the serum chloride, than that found

TABLE 2

RELATIONSHIP BETWEEN CONCENTRATIONS OF CHLORIDE AND PROTEIN IN VARIOUS BODY FLUIDS OF A PATIENT WITH CONGESTIVE FAILURE

	Protein	Chloride	Excess Protein In Serum (Serum-Fluid)	Excess Chloride In Fluid (Fluid-Serum)
	Gm. per 100 cc.	Mgm. per 100 cc.	Gm. per 100 cc.	Mgm. per 100 cc.
Serum	5.1	364		
Ascitic Fluid	0.9	387	4.2	23
Chest Fluid	0.7	389	4.4	25
Subcutaneous Edema Fluid	0.4	392	4.7	28
Cerebrospinal Fluid	0.02	436	5.1	72

*Synovial fluid has been included here since data accumulated by Dr. Walter Bauer (personal communication) suggest that this fluid is essentially a dialysate.

†These "in vivo" dialysates were obtained by Greene and Power[15] through an ingenious method whereby an ultrafiltrate of serum was secured through an artificial membrane interposed in the arterial path of the blood stream of dogs.

in the different edema fluids. Although the cerebrospinal fluid contained only 0.4 Gm. per cent less protein than the subcutaneous edema fluid, it contained 44 mg. per cent more chloride (table 2). In contrast, the subcutaneous edema fluid contained only 5 mg. per cent more chloride than the ascitic fluid, with a protein concentration 0.5 Gm. lower.

The observed ratio* describing the distribution of chloride between serum and certain body fluids, the excess of protein in the serum, and the distribution ratios calculated according to Van Slyke, Wu and McLean[18] to conform to the Donnan equilibrium equation are given in table 3. The values for the distribution of chloride between serum and cerebrospinal fluid reported by Muntwyler and his associates[10] and by Fremont-Smith and Dailey[19] are considerably lower than the theoretical Donnan ratios (table 3). The ratios found by these authors are similar to those reported by others[20, 21, 22, 23]. The observed chloride distribution ratios obtained for edema fluids (table 2) agree much more closely with the theoretical Donnan ratios, being the same as or slightly higher than the theoretical ratios.

As an explanation for the discrepancy between the observed and the theoretical ratios describing the distribution of chloride between serum and cerebrospinal fluid it has been pointed out[19] that a considerable amount of the plasma water may be bound to the protein or other colloids of the plasma. By assuming a value of 4.3 cc. of water per 100 cc. of plasma so bound, the discrepancy was obliterated[19]. However, this assumption seems invalid, since its introduction in the case of edema fluids and lymph would make the concentration of chloride in the "free" water of the serum higher than the concentration of chloride in these dialysates, a finding quite contrary to the Gibbs-Donnan law.

*In each instance the ratios express values calculated in relation to the water content of the serum and fluids.

It has been noted, by comparison of average values, that the cerebrospinal fluid chloride diminishes as the protein of the serum diminishes[13, 24]. This relationship is evident in figure 1, where the cerebrospinal fluid chloride excess is less for the series with low serum proteins than for the series with higher serum proteins. A diminishing cerebrospinal fluid chloride excess with a diminishing serum protein excess is in accord with the findings for dialysates. However, the chloride excess in the cerebrospinal fluid from patients with low plasma proteins is still much too great to comply with the excess of chloride found in edema fluids drawn from patients with low plasma proteins (figure 1). Further, an analysis of data in the literature[21, 22, 23] on the distribution of chloride and protein between cerebrospinal fluid and serum shows that the variations in individual instances from the average value for the cerebrospinal fluid chloride excess for a given serum protein are very great. It is not uncommon to find differences in the chloride excess of normal cerebrospinal fluids of as much as 20 mg. per 100 cc. in different patients with the same serum protein concentration, whereas an excess of chloride of this magnitude should, on the basis of edema fluid studies, correspond to a serum protein difference of some 4 or 5 Gm. per cent.

The cerebrospinal fluid chloride concentration and the serum chloride concentration are reduced in meningitis[13, 20]. The total osmotic pres-

TABLE 3

COMPARISON OF THE CHLORIDE DISTRIBUTION RATIOS FOUND WITH THE CALCULATED DONNAN RATIOS FOR VARIOUS BODY FLUIDS

Chloride Distribution		Author	Protein Difference (Serum-Fluid)	Ratio Found	Theoretical Ratio
Venous Serum / Spinal Fluid	(Dogs)	Muntwyler[10]	6.4	0.86	0.94
Venous Serum / Spinal Fluid		Fremont-Smith[19]	7.0*	0.88	0.93
Venous Serum / Ascitic Fluid		Greene[7]	5.2	0.97	0.95†
Venous Serum / Edema Fluids		Gilligan[2]	5.0	0.98	0.96
Venous Serum / Ascitic Fluid		Muntwyler[10]	—	0.96	0.96

*Serum protein value not given; taken to be normal.
†Value approximated by us from protein difference.

sure of the serum and cerebrospinal fluid, as measured by the freezing-point depression, are also reduced in meningitis[3]. The relative reductions of the spinal fluid chloride are at times greater than the reduction of the serum chloride so that the distribution ratio

$$\frac{\text{(Cl) serum}}{\text{(Cl) spinal fluid}}$$

may become more like that found in the case of edema fluids[20].

Stary, Kral and Winternitz[20] and Kral, Stary and Winternitz[25] found that the chloride concentration of the cerebrospinal fluid diminishes when the serum and cerebrospinal fluid of a patient are dialyzed against one another through a collodion membrane. After dialyzing, the difference between the chloride concentration of the serum and cerebrospinal fluid becomes approximately that found between serum and low protein edema fluids. As early as 1921 Mestrezat[26] showed that the chloride concentration of an artificial dialysate is less in respect to the serum chloride than the chloride concentration of cerebrospinal fluid.

Since physiological conditions are not reproducible outside the body, the fact that "in vitro" dialysates of serum from a given patient contain less chloride than the cerebrospinal fluid from the same patient has not, in the past, been considered important evidence against the dialysate nature of cerebrospinal fluid. However, comparative analyses made on the basis of the physiological equilibrium found between serum and edema fluids also lead one to the conclusion that the chloride concentration of cerebrospinal fluid is too high in respect to the serum chloride to accord with the dialysate theory of the nature of cerebrospinal fluid.

BICARBONATE

Hamilton[21] and Muntwyler[10], employing venous sera, and Linder and Carmichael[27], employing arterial sera, found that the average bicarbonate concentration of the cerebrospinal fluid is lower than the average bicarbonate concentration of the serum. According to the physicochemical laws of equilibrium, the bicarbonate concentration of a dialysate should be greater than that of the serum representative of equilibrium conditions. Muntwyler[10] found an average ratio

$$\frac{\text{(HCO}_3\text{) venous serum}}{\text{(HCO}_3\text{) spinal fluid}}$$

of 1.18 as compared with an average ratio

$$\frac{\text{(Cl) venous serum}}{\text{(Cl) spinal fluid}}$$

of 0.86 and a calculated Donnan ratio of 0.94 for the same series.

The studies in the foregoing paper[2] on the distribution of bicarbonate between serum and edema fluids show that the average bicarbonate concentration of edema fluids is greater than that of arterial blood and usually slightly less than that of venous blood. The average ratio

$$\frac{\text{(HCO}_3\text{) arterial serum}}{\text{(HCO}_3\text{) edema fluids}}$$

was 0.91, the average ratio

$$\frac{\text{(HCO}_3\text{) venous serum}}{\text{(HCO}_3\text{) edema fluids}}$$

was 1.01, and the ratio of serum of a bicarbonate composition midway between that of arterial and that of venous blood to edema fluids was 0.96 in a series where the average calculated Donnan ratio was 0.955. The value for the average bicarbonate ratio when venous serum was employed agrees with the ratios found by other investigators[7, 8, 10]. A consideration of the ratios found when both arterial and venous sera were employed indicates that HCO_3 is distributed between serum and edema fluids according to Donnan's law[2].

Greene and Power[15] obtained an average ratio

$$\frac{\text{(HCO}_3\text{) serum}}{\text{(HCO}_3\text{) dialysate}}$$

of 0.966 in their "in vivo" dialysate experiments, where the theoretical Donnan ratio was 0.933 and the blood sample representative of equilibrium conditions was known.

Muntwyler[10] suggested that the bicarbonate ratio for spinal fluid might accord more closely with the theoretical Donnan ratio if arterial rather than venous serum were compared with spinal fluid. When the results of Muntwyler[10] are estimated in terms of arterial serum, the bicarbonate concentration of the arterial serum is still considerably higher than the bicarbonate concentration of the cerebrospinal fluid. Further, Linder and Carmichael[27] found, on analysis of arterial serum and cerebrospinal fluid in patients with nephritic acidosis, that the bicarbonate concentration of arterial serum is considerably higher than that of spinal fluid.

These studies on the distribution of bicarbonate between serum and cerebrospinal fluid indicate that, unlike edema fluids, the bicarbonate concentration of cerebrospinal fluid is too low to accord with the distribution expected for a dialysate in equilibrium with plasma. The low cerebrospinal fluid bicarbonate concentration cannot be explained by assuming that bicarbonate is bound in the serum, since our data on the distribution of bicarbonate between serum and edema fluids[2] and the findings of Greene and Power[15] indicate that the bicarbonate of the serum is freely diffusible.

INORGANIC PHOSPHATE

The inorganic phosphate concentration of normal cerebrospinal fluid is approximately 60 per cent less than the inorganic phosphate concentration of the serum[20, 23, 28]. The cerebrospinal fluid phosphate increases proportionately with the serum phosphate increase in nephritis, so that the ratio of the concentrations remains approximately the same as normally[29]. On the other hand, the cerebrospinal fluid phosphate is not increased when the serum phosphate is increased in idiopathic hypoparathyroidism[30] and is not decreased when the serum phosphate is decreased following the administration of parathyroid extract[31]. In meningitis the cerebrospinal fluid phosphate may increase so that the ratio of cerebrospinal fluid to serum phosphate is increased considerably above the normal value[28].

The phosphate concentration of edema fluids[2, 7, 31], and of lymph[11] on the other hand is approximately the same as the serum phosphate concentration. In our studies[2] the average ratio of serum phosphate to edema fluid phosphate, calculated on the basis of water contents of the serum and fluids, was 1.03. In Heim's studies[12], the average ratio of the plasma to lymph phosphate was 0.98.

Walker[32], Pincus and his associates[33] and Ellsworth[34], employing ultrafiltration through artificial membranes, likewise found the phosphate concentration of serum and ultrafiltrate to be practically the same. Stary and his associates[20] observed that when cerebrospinal fluid is dialyzed against serum the cerebrospinal fluid phosphate increases, the concentration in the serum and cerebrospinal fluid being approximately equal at equilibrium.

Walker[32] recently observed that the concentration of inorganic phosphate in the cerebrospinal fluid and the aqueous humor of frogs is only 40 per cent of the concentration in the plasma, whereas the inorganic phosphate concentration of the frog lymph drawn from peripheral channels is approximately the same as that of the plasma. The inorganic phosphate concentration of glomerular urine is likewise approximately the same as that of plasma[35].

The fact that the normal cerebrospinal fluid inorganic phosphate concentration is only 40 per cent of that of the serum, whereas the inorganic phosphate concentrations of "in vitro" and "in vivo" dialysates and ultrafiltrates are approximately equal to that of the serum, speaks against the dialysate theory of cerebrospinal fluid.

The discrepancy in the phosphate values which have been found between cerebrospinal fluid and "in vitro" ultrafiltrates has been interpreted by Cantarow[29] as due to a distinct difference between the diffusibility of artificial and of living membranes. This interpretation becomes untenable in the light of the equal distribution of phosphate found between serum and edema fluids, lymph and glomerular urine. Further, to ascribe the low phosphate concentration of cerebrospinal fluid to a selective membrane permeability, as differing from the permeability of other living membranes seems untenable, especially in the light of the constancy of the cerebrospinal fluid inorganic phosphate concentration at different levels of the plasma phosphate concentration in hypo- and hyperparathyroidism.

SODIUM

In a large series of carefully controlled studies Fremont-Smith and Dailey[19], and Dailey[36] have shown that the concentration of sodium in the water of the cerebrospinal fluid is lower than the concentration of sodium in the water of the serum. Dailey[36] found that changes in the serum sodium concentration were reflected by changes in the cerebrospinal sodium concentration, and that the ratio of spinal fluid sodium to serum sodium tended to be constant.

Fremont-Smith and Dailey[19] found an average observed ratio

$$\frac{\text{(Na) spinal fluid}}{\text{(Na) serum}}$$

of 0.96 as against an average calculated ratio of 0.93 in twenty-five cases in which the cerebrospinal fluid was essentially normal in composition. Using the same analytical method as is used by these authors we found the average distribution ratio of sodium between edema fluids and serum to be 0.96[2] as against a calculated ratio of 0.955. Greene and his associates[7] also found an average ratio

$$\frac{\text{(Na) edema fluids}}{\text{(Na) serum}}$$

of 0.96 in a series for which the theoretical ratio was approximately 0.97.

From these data it would appear that the agreement is closer between the observed and calculated sodium ratios for edema fluids than for cerebrospinal fluid. The differences between the observed and calculated ratios for cerebrospinal fluid are not great, however. Fremont-Smith and Dailey[19] pointed out that if one assumes that approximately 4 per cent of the plasma water is "bound," this difference for cerebrospinal fluid can be eradicated. For the reasons mentioned previously, this assumption seems invalid.

CALCIUM

The calcium concentrations of normal cerebrospinal fluid and of edema fluid are considerably less than the calcium concentration of serum.

The large excess of serum calcium over edema fluid calcium is ascribed to the affinity of protein for this ion, a calcium-protein combination resulting, which is non-diffusible both through capillary and collodion membranes.

The calcium concentration of normal cerebrospinal fluid averages approximately 50 per cent of the normal serum calcium concentration[22, 25, 28, 37]. A large number of the reported serum ultrafiltration and dialysis experiments performed "in vitro", and the "in vivo" dialysate studies of Greene[15] give values for the diffusible calcium which are somewhat higher than the cerebrospinal fluid calcium values. Likewise, the calcium concentrations of low protein edema fluids[2, 7, 8] indicate that approximately 70 per cent of the serum calcium is diffusible.

In meningitis the cerebrospinal fluid calcium is often increased above the normal[28]. As was pointed out by Merritt and Bauer[28] the increase in the cerebrospinal fluid protein concentration in certain meningitis cases may account satisfactorily for the increase in the cerebrospinal fluid calcium concentration. In other cases the increases are not accounted for in this manner, and would, according to these authors, seem to be a result of the pathological changes in the meninges and choroid plexus.

Kral and his associates[25] showed in one experiment in which serum was dialyzed against cerebrospinal fluid that the calcium concentration of the cerebrospinal fluid increased from 48 per cent to 65 per cent of the serum calcium concentration.

It has been shown that the cerebrospinal fluid calcium does not increase appreciably when the serum calcium increases during parathormone administration[31, 38, 39]. Further, the cerebrospinal fluid calcium does not decrease appreciably in parathyroid tetany when the serum calcium concentration is strikingly decreased[30]. Albright and his associates[30] have reported studies on a patient with idiopathic hypoparathyroidism in whom the serum and cerebrospinal fluid calcium concentrations were identical, each being 4.5 mg. per 100 cc.

In contrast to these findings, the calcium concentrations of edema fluids of low protein concentration[31] and of lymph[12] show practically the same increase as the calcium concentration of serum during parathormone administration. Arnold and Mendel[12] have further shown that the lymph calcium is decreased as is the serum calcium after parathyroidectomy. These results lead one to conclude that the administration of parathormone causes an increase in the physiologically diffusible calcium fraction of the serum[31]. This conclusion is directly opposite to the conclusion to which one is led if one accepts cerebrospinal fluid as a representative physiological dialysate[38, 39]. Peters[40] likewise concludes that the logical inference from these conflicting results[12, 38, 39] would be that spinal fluid is not a simple dialysate. He states that if cerebrospinal fluid were to be considered a dialysate the only alternative would be that lymph is not a dialysate, a conclusion against which there is an overwhelming body of evidence.

MAGNESIUM

According to Barrio[41], and to Stary, Kral and Winternitz[42], the magnesium concentration of cerebrospinal fluid averages approximately 40 per cent higher than the magnesium concentration of serum from the same patient. In contrast, Greene and his associate[15] found that the magnesium concentration of the "in vivo" dialysate was lower than that of the serum. Likewise, Greene and his associates[7] found that the magnesium concentration was lower in transudates than in the corresponding sera. The values for the distribution ratios found by these authors[15, 7] indicate that the serum magnesium concentration is higher than that of the dialysates and transudates partly by virtue of the Donnan laws of distribution and partly because of a bound magnesium compound in the serum, comparable to a bound calcium compound.

Stary, Kral and Winternitz[42] further found that when cerebrospinal fluid was dialyzed against serum from the same patient, the magnesium concentration of the cerebrospinal fluid became lower than that of the serum. The same analytical method was used for the cerebrospinal fluid before dialyzing and for the dialyzed cerebrospinal fluid.

Whereas according to physicochemical laws and to the values found for edema fluids[7], the concentration of magnesium should be lower in plasma dialysates than in the plasma, the concentration of magnesium in cerebrospinal fluid is, according to the above-mentioned investigators[41, 42], higher than the concentration in the plasma.

NON-PROTEIN NITROGEN CONSTITUENTS

The total non-protein nitrogen concentration in cerebrospinal fluid is approximately 60 per cent of the concentration in the serum[23, 43]. In contrast, the total non-protein nitrogen concentrations of edema fluids[2] and of lymph[11] are, when calculated on the basis of water content, approximately equal to the concentrations in the sera. This latter relationship accords with the dialysate nature of edema fluids and lymph, and indicates that the membranes separating these fluids from the plasma are permeable to all of the plasma non-protein nitrogen constituents. Approximately equal creatinine distribution between serum and edema fluids[2] and approximately equal distribution of urea between serum and lymph[11] have been demonstrated.

The low values obtained for the total non-protein nitrogen constituents of spinal fluid are apparently the resultant of the almost complete absence of uric acid[43, 44] and the low values for creatinine[43, 44] and for amino acids[45]. The values reported for the distribution of urea between cerebrospinal fluid and plasma are conflicting[44, 46, 47] probably due to the utilization of incorrect analytical methods in certain instances. The results of Galan and Houssay[47] however, demonstrate practically equal concentrations of urea in blood, spinal fluid, lymph, pancreatic juice and bile in the dog. Cahane and Henrich[46] have also shown in a recent study of a large series of cases that the cerebrospinal fluid and serum urea concentrations are usually similar.

The above similarities and differences in the distribution of the various non-protein nitrogen constituents of body fluid dialysates (edema fluids and lymph) and serum, and cerebrospinal fluid and serum, do not offer convincing proof either of the dialysate or of the non-dialysate theory of the nature of cerebrospinal fluid. The almost complete absence of uric acid and the low concentrations of creatinine and amino acids might conceivably be attributed to a selective permeability of the membrane separating the cerebrospinal fluid from the plasma. This seems improbable, however, especially in the case of the amino acids. The similarity in the concentration of urea in the cerebrospinal fluid and serum does not necessarily favor the dialysate theory, since urea is likewise distributed practically equally between pancreatic juice and serum, and bile and serum[47].

SUGAR

Under fasting conditions, cerebrospinal fluid normally contains approximately 60 per cent of the total reducing substances of the serum. Fremont-Smith and his associates[23] found in 22 adult patients that the normal cerebrospinal fluid sugar varied from 49 per cent to 81 per cent of the blood sugar and Stewart[14] found variations from 42 per cent to 82 per cent in thirty normal infants and children. The cerebrospinal fluid sugar is increased when the blood sugar is increased after a meal[48] and in diabetes[49], and decreased after insulin[50].

Ventricular fluid contains, according to Stewart[14], approximately 6 mg. more sugar than lumbar fluid, and fluid from the cisterna magna contains on the average 1 mg. more sugar than lumbar fluid, indicating that sugar is oxidized in the spinal canal.

By a comparison of data found by Somogyi's sugar method[51] with that found by the Folin-Wu method[52], Cohn, Levinson and McCarthy[53] conclude that the cerebrospinal fluid contains an average of 8 mg. per 100 cc. of non-glucose reducing substances. Using Somogyi's method Cohn further found that the cerebrospinal fluid glucose concentration averaged 88 per cent of the whole blood glucose concentration. Transposing Cohn's figures to terms of concentration per unit of water content of cerebrospinal fluid and whole blood, the difference in the glucose concentration of the two fluids becomes much greater.

Equality of glucose concentration in lumbar or ventricular fluid and plasma has not, to our knowledge, been demonstrated.

The concentration of reducing substances in edema fluids, on the other hand, is the same or slightly greater than the concentration in the serum when the values are calculated on the basis of the water content[2]. Reasons were given in our previous communication for believing that in those cases where the edema fluid sugar was slightly higher than the serum sugar, true equilibrium was not obtained. Power and Greene[54] likewise found approximately the same concentration of total reducing substances in plasma and in the "in vivo" dialysate and concluded from their results that glucose is diffusible and that there is no evidence of a non-diffusible or colloidally bound form of sugar in the plasma. Equality of glucose concentration in serum and its dialysates must then be expected.

The apparent discrepancy in the distribution of sugar between plasma and cerebrospinal fluid has been explained, as pointed out by Walker[32] on two bases: (1) a portion of the plasma sugar is in a form which is not filtrable through the membrane separating spinal fluid from plasma, and (2) a portion of the plasma sugar is utilized by the brain tissue before the fluids to be analyzed are collected.

Walker[32] found that the cerebrospinal fluid and aqueous humor of the frog also contained on the average only 60 per cent of the sugar of the plasma, whereas the sugar of the web lymph and the glomerular urine[35] of the frog was approximately equal to that of the plasma. This author points out that since only 5 mg. per 100 cc. of a total of approximately 40 mg. per 100 cc. of reducing substances in frog plasma represent non-fermentable sugar, the cerebrospinal fluid of the frog contains considerably less fermentable sugar than the plasma. Walker[32] further concludes, "The failure of cerebrospinal fluid sugar to approximate the plasma level after preliminary cisternal drainage (in the frog) argues against the sugar utilization hypothesis which is finally rendered untenable by the demonstration that this deficiency is maintained in depancreatized dogs, whose sugar utilization must be greatly diminished or abolished."

The distribution of sugar between cerebrospinal fluid and serum differs, therefore, from the distribution found between serum and body fluid dialysates or ultrafiltrates, such as edema fluids, lymph and glomerular urine. This apparent non-conformity of the cerebrospinal fluid

sugar distribution with that found for dialysates cannot be entirely explained on the bases of non-diffusibility of the plasma sugar or of modification of the cerebrospinal fluid sugar concentration by tissue oxidation subsequent to dialysis.

DISCUSSION

The validity of the dialysate theory of the nature of cerebrospinal fluid has been tested by a comparative analysis of the reported distribution of substances between serum and cerebrospinal fluid and the distribution of the same substances between serum and edema fluids. It has been pointed out in the preceding communication that edema fluid is, beyond reasonable doubt, a simple dialysate in equilibrium with plasma. The comparison between the distribution of substances between serum and cerebrospinal fluid and serum and edema fluids has been amplified by reference to the results reported in the literature for the distribution of substances between serum and lymph and serum and artificial dialysates, as well as by repeated reference to the recognized physicochemical laws for dialysates.

The distribution of chloride, bicarbonate, inorganic phosphate, sodium, calcium, magnesium, non-protein nitrogen constituents and the reducing substances has been discussed. The other constituents of the plasma have not been taken up because there are not sufficient reliable data available on the distribution between serum and the body fluids in question. The results of the many investigators who have measured the relative serum and cerebrospinal fluid concentrations of the substances discussed are essentially in accord with one another.

This study has revealed that the distribution of many substances between serum and cerebrospinal fluid differs markedly from the distribution between serum and edema fluids, lymph and artificial dialysates. The corollary to this is that the distribution of substances between serum and cerebrospinal fluid differs markedly from the distribution demanded by the physicochemical laws of dialysates. It has been pointed out that erroneous conclusions concerning the physiological diffusibility of the constituents of the plasma have been drawn because cerebrospinal fluid has been considered a representative physiological dialysate.

Evidence, on the basis of chemical studies, that cerebrospinal fluid is neither a dialysate nor a simple ultrafiltrate has also been advanced recently by Stary and his associates[42], by Peters[40], and by Walker[32].

SUMMARY

1. The validity of the dialysate theory of the nature of cerebrospinal fluid has been tested by comparing the distribution, as reported in the literature, of substances between cerebrospinal fluid and serum with the distribution of the same substances between edema fluids and serum. This comparison has been strengthened by reference to the physicochemical laws of equilibrium and to the reported studies on lymph and artificial dialysates.

2. The distribution of chloride, bicarbonate, inorganic phosphate, calcium, magnesium, non-protein nitrogen constituents, and reducing substances between serum and cerebrospinal fluid differs importantly from the distribution of these same substances between serum and edema fluids. The distribution of sodium differs only slightly.

3. The factors which might explain these discrepancies in favor of the dialysate theory of cerebrospinal fluid have been considered and found inadequate.

4. It must be concluded that cerebrospinal fluid is not a dialysate or a simple ultrafiltrate.

5. The consideration of cerebrospinal fluid as a representative physiological dialysate or ultrafiltrate has led to erroneous conclusions concerning the general physiological diffusibility and chemical state of constituents of the plasma.

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FRANCE HONOURS RESEARCH

The President of the French Republic has paid a notable tribute to medical and chemical research by conferring the honour of La Croix de Chevalier de la Légion d'Honneur upon Sir Henry Wellcome, LL.D., F.R.S., the Founder of the Wellcome Research Institution and its associated research laboratories and museums, in which are included The Bureau of Scientific Research, Physiological, Chemical and Entomological Research Laboratories, and The Museum of Medical Science and The Historical Medical Museum.

Sir Henry Wellcome is a native of Wisconsin and was graduated at the Philadelphia College of Pharmacy. He is President of Burroughs Wellcome & Co. (U. S. A.), Inc., New York, in whose research and experimental laboratories much original work has been done.

NEW ENGLAND BRANCH, AMERICAN UROLOGICAL ASSOCIATION

SOME DEPARTURES FROM THE BEATEN PATH IN KIDNEY SURGERY*

Experimental Studies

BY NELSE F. OCKERBLAD, M.D.†

AFTER watching the remarkable work of O. J. Dixon[1, 2] in live muscle transplants in veins and in liver and spleen tissue, I begged his consent to extend this work to the field of kidney surgery and it is with his kind permission that I have been able to pursue these studies and present to you these findings. Not only are these studies and experiments intensely interesting but they are, I believe, capable of a very wide clinical application in human surgery. The use of freshly cut pieces of muscle as a hemostatic is not entirely new. The use of viable muscle grafts and implants is quite new so far as it has been extended to veins and arteries by Dixon and to kidney surgery by me.

Harold Neuhof[3] in his monograph in 1923 said, "The free transplantation of striated muscle is not a method of established usefulness in surgery. Except for its hemostatic properties muscle as a transplant has proved of little clinical value. The first work to appear on the subject was a publication by Zielonko in 1874, who transplanted muscle tissue into the lymph sac of a frog and noted the rapid necrosis of the graft without any evidence of regeneration." Neuhof states that experimentally Laewen[4] was the first to demonstrate that fresh muscle tissue could be successfully used for the control of oozing from parenchymatous organs. Laewen and Jurasz[5] report two successful cases where wounds of the heart were sealed with a piece of fresh muscle tissue. Earlier than this, however, Harvey Cushing[6] made use of bits of the temporal muscle freshly cut out and placed upon the oozing points in the exposed brain. He thought that his observation was entirely original, but when he found that Sir Victor Horsley[7], the noted English brain surgeon, had preceded him, he gave him credit in a footnote. Sir Victor had been using it for years but only published a short note upon the subject in 1914. The first and only known man other than Dixon to use viable muscle grafts was Harold Kisch[8], who used the live muscle graft in a mastoid operation to control the oozing from the bone. Harvey Cushing's[6] observations were unique and interesting. He found that in brain operations the gauze tips or pledgets of cotton used to sponge adhered to the tissue and when removed the bleeding again started. Casting about for something to leave in the wound he tried cutting pieces of the temporal muscle and found that these would adhere very promptly and check further extravasation better than the gauze or cotton pledgets. He also found that by saving the blood clots that resulted from the hemorrhage after going through the scalp and skull, he could make use of these as a hemostatic. This interesting observation is quoted because of its bearing upon another equally interesting contribution of Eugen Joseph[9] of Berlin, who published a valuable paper on the subject of muscle implantation in nephrotomy in 1931. Joseph freely states that he got his idea some years before from watching Harvey Cushing using the muscle tissue for hemostasis in brain operations and says that he set his Italian assistant Ciminata[10] to work on the problem as it might relate to the kidney in dogs. Ciminata published his observations in 1924. This was the first work using muscle tissue to control bleeding in kidney operations, but it was all done on non-viable muscle. Ciminata used eighteen dogs in his experiments and in most instances the convex surface of the kidney was resected and in one instance the lower pole was resected. His method was to place the muscle tightly on the bleeding surface and suture it securely in place with fine catgut. About six sutures were taken to fasten the muscle in place. Of the 18 dogs, 13 died, one from peritonitis, three from shock, and nine from suppuration in the region of the kidney. From the five dogs which lived, the following data were compiled. In three days, the muscle tampon had a rough appearance, no bleeding. In six days the muscle tissue could not be seen. The parenchyma wound was covered with a grayish colored slough. In ten days there was a depression of a fibrillar appearing tissue. In 15 days healing was completed; in 20 days, a scarred depression; in 62 days only a superficial scar. The histological findings were interesting and he states that when necrosis of the muscle occurred there was an infiltration of the kidney parenchyma, of the kidney capsule, and of the fat capsule of the kidney. The kidney tissue showed an increase in the intertubular stroma, an enlargement of the uriniferous tubules to-

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gether with hyaline casts, and in a few places anemic necrosis. There was no evidence of regeneration of the muscle fibers. He concluded that if careful asepsis were practiced, it would be possible to secure rapid healing of the kidney after muscle transplant. On the basis of this work of Ciminata, Eugen Joseph[9] applied gut sutures. This he says will act as a tampon to prevent bleeding.

In 1917 a very important paper was published from the Laboratory of Surgical Research of the Harvard Medical School by Edward H. Risley[11] and although this paper long preceded Eugen Joseph's publication and Ciminata's con-

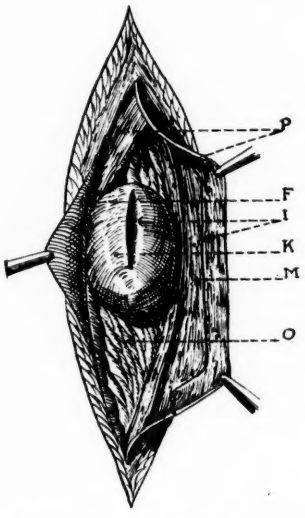

FIGURE I. Showing incision into the kidney ready to receive the muscle implant.

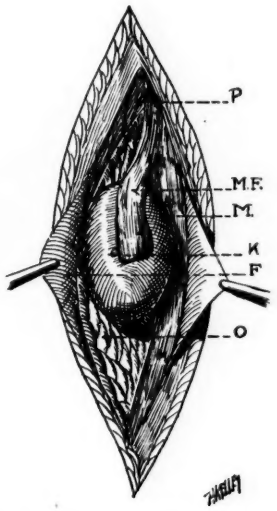

FIGURE II. Showing viable muscle graft pressed down into the wound, sealing it and controlling hemorrhage. No suture used.

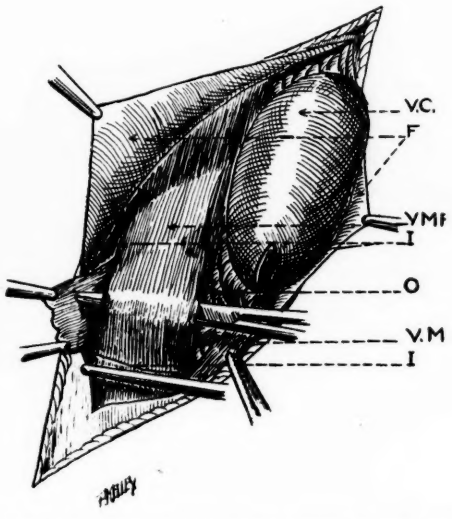

FIGURE III. Wedge-shaped piece resected from lower pole of kidney.

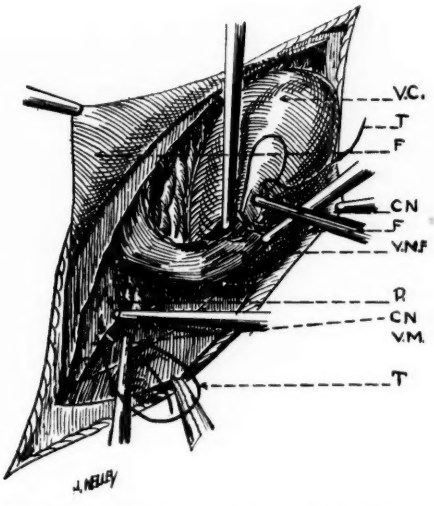

FIGURE IV. Viable muscle flap applied to the wound—one suture used to hold it in place.

it to operations upon the kidney in human beings, particularly in cases of nephrotomy for stones in solitary kidneys where there was danger of hemorrhage, and in 1931 reported five cases in which muscle was placed in the nephrotomy wound to control bleeding. He concludes that since nephrotomy has a rather high mortality due to postoperative hemorrhage (8 to 10 per cent in his experience) he proposed to use a piece of the lumbosacral muscle cut the size and shape of the kidney wound and pressed into it and lightly fixed by a few cat-

tribution it was apparently overlooked by both of them as no reference was made to it by either. Risley's work consisted of 12 experiments on dogs, five of which were upon the kidney, three using muscle, one fascia, and one fat. He found that histologically the line of contact of muscle tissue against bleeding surfaces showed an excess of blood platelets and fibrin in considerable degree five to ten minutes after the application and rightly states that its value lies largely in its thrombokinetic content. From his twelve experimental studies he concludes:

1. The ideal hemostatic in wounds of parenchymatous origin is interposed muscle tissue taken at the time of operation from the patient's own body.
2. Such muscle in order to most effectively stimulate fibrin formation should be jaggedly cut with a knife, not crushed as with scissors, nor should its hemostatic properties be extracted by its contact with salt solution.
3. Fascia and fat act to a more limited degree as hemostatics.

After seeing the remarkable properties exhibited by the viable muscle grafts, I was very anxious to try some experiments with particular reference to the kidney. The work presented here is only a preliminary report on a problem which we expect to work and report on from time to time through the years without perhaps exhausting all of its possibilities. Possibly you will bear with me while I present to you a rather fragmentary study of a subject that seems to me to be of tremendous importance to us as urologists.

EXPERIMENT NO. I

The left kidney of a 10 kg. dog was exposed and lifted out of the wound. An incision one half the length of the kidney (3 cm.) was made 2 cm. deep into the kidney in the midline extending well into the parenchyma of the kidney causing profuse hemorrhage. The bleeding was temporarily controlled by finger pressure upon the renal artery. The live muscle graft which had been prepared from the latissimus dorsi muscle 6½ cm. long and 2 cm. wide was then pressed into the kidney wound and held in place with the fingers for three minutes. The pressure upon the pedicle was released and all bleeding had been stopped by the live muscle graft which had tightly adhered to the wound. No sutures whatever were used to hold the graft in the kidney incision. The kidney was placed gently back in the abdomen and the wound closed in layers. This dog died 20 hours later of the sodium amytal anesthesia. Examination of the operated area revealed no hemorrhage. The muscle graft was densely adherent to the kidney wound, completely obliterating it. The tremendous flow of blood occasioned by so large an incision into the kidney parenchyma and the ease with which the live muscle graft controlled it was a rather dramatic procedure. It was remarkable that the hemorrhage was completely controlled within a space of three minutes and that without the aid of sutures. All other experimenters using nonviable muscle grafts have made use of sutures to hold their tissues in place.

EXPERIMENT NO. II

This was quite similar to the first except that the wound in the left kidney was larger and the live muscle graft longer. The kidney pedicle was compressed with the fingers and the viable muscle graft was pressed into the wound in the kidney. In this case the kidney incision was so large that the prepared muscle graft did not quite cover the edges of the wound so that pressure had to be maintained for eight minutes before the pedicle could be released and we were sure of complete hemorrhage control. The kidney was gently replaced in the abdomen and the wound closed in layers leaving the muscle graft passing through the abdominal wall and into the peritoneum. This dog was not sacrificed until 60 days later when it was found that there had been neither infection nor hemorrhage and the muscle graft had not degenerated in any way and it still adhered to the kidney.

EXPERIMENT NO. III

The left kidney of a 17.5 kg. dog was exposed by a loin incision. A piece of live muscle was prepared 7 cm. in length and made ready for use. The kidney was delivered and an incision 2 cm. long was made, cutting out a wedge-shaped piece out of the lower pole of the kidney. The muscle graft was spread out flat over this wound and pressed down into it. After five minutes the graft adhered and the hemorrhage ceased. Due to the position of the graft in relation to the kidney wound it was feared that the graft might be peeled out of the wound when the kidney was replaced, so a single mattress suture was placed to prevent this from happening. The dog completely recovered from the operation.

EXPERIMENT NO. IV

In a 10 kg. dog, the right kidney was exposed. A viable muscle graft 8 cm. long was prepared from the external oblique. The kidney was split from pole to pole down to the kidney pelvis. The muscle graft was pressed down into the wound while holding the pedicle compressing it with the fingers. After two minutes the pedicle was released and the blood welled up from the wound. Pressure was maintained for another four minutes when it was again released. This time the bleeding was controlled. No sutures were used. The dog was sacrificed 60 days later because of distemper. The muscle graft was still good and showed no signs of degeneration.

EXPERIMENT NO. V

Dog No. 43. A left rectus incision was made 12 cm. in length. A piece of the left rectus muscle was prepared as a viable muscle graft. The left kidney was then delivered out of the wound and an incision made cutting off the lower third of the kidney. The pedicle was compressed with the fingers and the viable muscle graft applied. The graft adhered promptly to the cut surface but was not quite large enough so that a supplementary smaller graft had to be added. This was not a viable graft. It adhered to the cut surface and in five minutes all bleeding had

ceased. The dog died 31 days later and the examination showed no apparent cause of death. The viable muscle graft was still in place and the muscle showed no degeneration. The nonviable piece had sloughed off and completely disappeared. There had been no hemorrhage and no infection.

EXPERIMENT NO. VI

Dog No. 39. The right kidney of a 16.3 kg. dog was exposed by a lumbar incision and delivered out of the wound. The pedicle was stripped of its fat and coverings so that the renal vein was exposed. A viable muscle graft was prepared from the external oblique. An incision was made into the renal vein with the point of a sharp knife 3 mm. in length. Blood poured out in a steady stream. The muscle graft was pressed down over the wound in the vein and it immediately adhered and the bleeding ceased within three minutes' time. Because of the fact that there seemed to be some tension on the viable muscle graft where the kidney was replaced, it was cut off from its attachment and placed back with the kidney. The dog recovered. No hemorrhage, no infection. The dog was killed because of a distemper epidemic among our animals 41 days later. The muscle had degenerated but was still adherent to the renal vein. This remarkable experiment had a practical application a short time later when, in the course of a rather complicated pyelotomy for a large stone in a human being, I accidentally injured the renal vein so that it was badly torn. I immediately made pressure on the vein while a muscle graft was prepared and applied the muscle to the wounded vein and made steady pressure for three minutes. The graft adhered and the bleeding ceased. The kidney was replaced and the patient recovered. I believe that, in injuries to the renal vein in the course of operative procedures, the application of live muscle to the wounded vein is a much simpler and very much safer procedure than an attempt to suture the vein. The second human case is one in which I did a nephrotomy for stone, having incised the lower pole of the kidney. A live muscle graft derived from the quadratus lumborum was prepared and placed in the wound and the wound closed over it by the usual means of chromic mattress sutures with pieces of fat in the loops to prevent cutting. I did not have quite the requisite courage to place the graft without sutures although I feel perfectly certain that it would have adhered as firmly as it did in the experimental animals. Eugen Joseph did not trust any of his nephrotomies without sutures. How far one may go in this direction, I hesitate to say without further experimental work. I am not yet advocating the interposition of muscle grafts, viable or non-viable, in human surgery even though in these two cases cited it seemed to be a safe procedure.

EXPERIMENT NO. VII

The next experiment was on a dog in which I had previously operated the left kidney. The right kidney was exposed by a lumbar incision and the kidney delivered. A live muscle graft 7 cm. in length was prepared from the external oblique muscle. The kidney was split down to the pedicle from pole to pole. The pedicle was compressed with the fingers and the thick muscle graft laid in the wound. The kidney was then bound together with Lowsley's ribbon catgut 5/8″ wide, one on either side of the hilus and these tied rather securely. The muscle graft contracted somewhat so that it seemed necessary to place one mattress suture near the end of the graft, spoiling what would otherwise have been a perfect demonstration of the usefulness of this unique closure method of Lowsley[12]. I was rather fearful that, in so complete a division of the kidney, nothing would prevent fatal hemorrhage, but the combination of the live muscle graft and Lowsley's bands prevented hemorrhage. This dog weakened and was ill so that 27 days later we sacrificed the animal and found that there were many adhesions to the surrounding organs. There had been no hemorrhage or infection. One of Lowsley's bands had completely disappeared. Parts of the second one could be seen not quite completely absorbed.

I feel certain that Lowsley has hit upon an idea that will prove of great value in kidney surgery and I intend to pursue the experimental work farther in this direction until I have some more definite data to present. So far this seems to promise much in the way of improved technique in nephrotomy. Much more remains to be done in this interesting and fertile field.

The applications that I see so far as they relate to the field of urology are many. In kidney surgery, I believe this method of live muscle grafts may have considerable application, particularly in nephrotomy. In blood vessel surgery, especially injuries to the renal vein or to the cava, it will replace attempts at suturing these fragile vessels in such difficult situations. In hemorrhage from the urethral bulb or even the prostatic bed, live muscle grafts can be freely used. In wounds of the corpora cavernosa or even the use of live muscle grafts in fibrosis of the corpora cavernosa to act as a framework upon which a new endothelial structure can be formed is not entirely visionary.

I have not touched upon the physiology of the remarkable hemostatic properties of live muscle tissue because that is pretty well known and much work has been done to attempt to explain all the processes, though our knowledge of these processes is not as yet complete. The pathology which the live muscle graft induces in the kidney wounds and the microscopic pictures are not yet complete but are being studied and will be presented at a later date.

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DISCUSSION

DR. WILLIAM C. QUINBY: I have been most interested in the presentation which Dr. Ockerblad has been kind enough to make to us; for it brings up for discussion many different phases of both physiology and surgery.

In the first place we have to deal with the question of the physiology of the coagulation of the blood which is still a rather abstruse matter. It is known that muscle tissue, when cut away from its support, is quick to produce coagulating substances. It is this which one takes advantage of in using muscle tissue for hemostasis.

Dr. Harvey Cushing, now Professor of Surgery at New Haven, once studied this question in detail. Inasmuch as fibrin is an element in the coagulation of blood he tried to devise various methods of applying fibrin, taking blood collected sterilely and whipping it into sheets of fibrin. We used these for a while in the laboratory at the Harvard Medical School and once or twice I used it clinically as a method of applying a quick styptic to parenchymatous bleeding. Unfortunately it was not successful. The fibrin acted as a foreign body so that the wounds did not heal by first intention though hemostasis was satisfactory. Muscle itself, however, does do exactly what Dr. Ockerblad has said. It promotes coagulation of blood. The factors which surround its successful use are several, however.

In the first place, the bleeding must not be too profuse. As Dr. Ockerblad has stated, bleeding must be controlled in the beginning by pressure on the renal pedicle. In other words, it is not possible to make an incision into the kidney and remove whatever is necessary or make for instance a heminephrectomy, without having previously prepared that kidney to such an extent that one has control over the vascular pedicle, because the mere force of the arterial bleeding will wash the muscle graft away so that it has no chance to act. Pressure, therefore, is a factor in controlling hemorrhage from such parenchymatous organs as the kidney, the liver and possibly the spleen, even more important than Dr. Ockerblad has suggested.

There are various other methods of controlling hemorrhage from the kidney of which one is the use of the high frequency elective current. For instance, having made the kidney sufficiently mobile to control the vascular pedicle, if one then opens the whole kidney by a complete or partial nephrotomy, controlling the vascular pedicle, actually picks up the important bleeders on very fine hemostats and then applies the high frequency electric current to the handle of the hemostat a sufficient control of the immediate hemorrhage will frequently be secured.

In closing I wish to congratulate Dr. Ockerblad on his splendid work.

DR. RICHARD CHUTE: May I ask Dr. Ockerblad when he discusses his paper if he will comment on whether there is any value whatsoever in non-viable tissue. I take it he means viable as attached at one end and I wonder if non-viable tissue has any value.

DR. J. H. CUNNINGHAM: What I have heard this evening impressed me particularly because it is a general principle rather than a procedure that is devoted entirely to our specialty. Any general principle, I think, that may be applied to our specialty is far more important.

Being conversant with the literature that Dr. Ockerblad has presented from time to time, I have always been impressed with one fact—he always seems to hit the nail on the head. I think his kidney clamp is a good example. Now when he comes with a general principle applied to something that we are all confronted with, although we have overcome our difficulties by methods already in use, this new principle of controlling kidney hemorrhage is certainly something that is a great addition to what we already know.

The conservation of kidney tissue has always been to my mind a very important thing, and the employment of mattress sutures to close kidney wounds has always been in my opinion a procedure which probably destroys considerable kidney tissue. We have been trying to get away from this by various improvements in technical procedures. The idea of implantation of fat with less suture in the kidney would, I think, have been helpful. Probably all here have had instances where the patient's general condition was such that we have tamponed the kidney incision without any suture, but with control of bleeding. I recall several instances where I have used the kidney elevating clamp, I believe it is called, to compress the kidney and stop hemorrhage. This clamp left for 24 hours obviates any suture. However, to have a general procedure such as we have heard of tonight for our use, advocated by somebody who has not too much theory, but a very definite viewpoint of practical application is, I think, of extreme importance. I am delighted to have had this new method of controlling kidney incision hemorrhage added to the various methods that I already employ.

DR. AUGUSTUS RILEY: I believe the speaker's ideas of hemorrhage control express great thought. In the past few years I have done partial nephrectomy in a few selected cases, and was able to control the hemorrhage without much, if any, difficulty with properly placed sutures. One case especially, I recall at the present time. A heminephrectomy was done and the hemorrhage was controlled very easily with deeply placed sutures. Apparently the half of the kidney left was not damaged to a great extent, because a split function, done some time after the operation, was good and compared well with the non-operated kidney in proportion to the amount of kidney tissue left at the time the heminephrectomy was done.

I agree with Dr. Cunningham, our method of hemorrhage control in kidney surgery may be rather crude in appearance, but it does the work.

I am glad to have heard the speaker's paper, am glad to know his method of controlling hemorrhage, and will certainly try it when the opportunity presents itself.

DR. GEORGE G. SMITH: I do not know of any paper which has been presented here that I can remember which has in it so much that may prove of value to men who are doing operative work on the kidney and doing general operative surgery. It seems to me that Dr. Ockerblad has brought forward here a new principle which will be more than helpful.

I would like to ask Dr. Ockerblad if he has any idea as to whether, in using this in a kidney in which there is sepsis, say after removal of a stone from a fairly septic kidney, the muscle graft would hold in the same way or whether the sepsis would be a factor operating against it.

DR. OCKERBLAD (In closing): Dr. Smith has raised the question of sepsis in connection with muscle implants and that is right in line with the query about live muscle grafts. One of the main points about live muscle grafts is that they apparently are not so subject to infection as the detached pieces of muscle. The detached muscle grafts are frequently the subject of infection. One of our workers did nephrotomies on six dogs and used detached muscle as implants in these nephrotomy wounds and three of the dogs developed infection. In over thirty other dogs we have had only one infection with live muscle grafts. Apparently the live muscle grafts have considerably greater resistance to infection.

In answer to the question which Dr. Smith has brought up as to whether we have tried them in infected wounds, I can only say that we have not done so as yet. We will have to deliberately make these infections in dogs and then implant muscle tissue to see what happens, but I fear that muscle tissue cut off this way from its blood supply will act as a culture media and will not aid in hemostasis so well as it would when still attached to its blood supply.

Dr. Quinby has been very complete in his discussion. His statement that fibrin had been a failure as a preparation in advance is perfectly true and I carefully avoided this whole subject inasmuch as there have been volumes written on it. There seems to be no end to it if one starts a discussion of the various theories of the formation of blood clot. However, these essential hemostatic agents cannot be prepared and stored up in advance. There must be something in the piece of live muscle or those freshly detached which those prepared juices do not have.

Pressure certainly has a marked effect in controlling hemorrhage in parenchymal tissue like the spleen, liver, and kidney although I think the kidney tissue is quite different from either spleen or liver and perhaps the bleeding in kidney tissue is a little more easily controlled than that in spleen tissue, but pressure was not a factor in the veins which Dixon opened and pulled the muscle strips through. The long live muscle grafts stopped the hemorrhage in that situation just as readily as they did in the kidney structure. Take the adherence of these muscle flaps to the vein and to the cava. In these places we used just enough pressure to make them stick fast and the graft adhered permanently in a very short time.

Dr. Chute's question about non-viable muscle tissue, I have perhaps covered.

There is much more work to be done on this very important subject and this presentation is merely a summary of the work we did last summer.

I want to thank you for your kind attention and your generous participation in the discussion.

WHERE THE DEATHRATE HAS INCREASED

On the basis of their crude deathrates three diseases, cancer, diabetes and heart disease, recorded higher mortalities in 1933 than ever before. The great bulk of the deaths from these diseases occurs among persons in the higher age ranges—specifically from age 55 on. Accordingly, it is necessary in considering the course of the deathrate from these conditions (especially with respect to what has transpired during recent years) to take into account a change that has occurred in the age distribution of Metropolitan Industrial policyholders as in the general population. There has been a shift whereby a larger proportion of the insured is finding itself in the higher age groups. This increase in the average age of this group, in itself, tends to raise the crude deathrate of these three diseases. Its effect, in fact, has been so marked that it is necessary to use standardized deathrates, which make allowance for changes in age distribution, in order to make valid comparisons of the 1933 deathrates with those of previous years. When standardized rates are prepared, we find that the 1933 cancer and diabetes deathrates are higher than ever previously recorded, although the rise is shown to have been by no means so sharp as the crude figures would indicate. The heart disease deathrate, on the other hand, is actually lower than for both 1930 and for 1911, the year in which the Metropolitan began to compute mortality rates for individual causes of death, and shows only a slight rise as compared with that for 1932.

When analysis of what has happened in recent years is extended to the several types of cardiac impairments, we find much that is encouraging in the trend of the heart disease deathrate. First, only in the higher age groups is the mortality increasing; and the heart disease prevailing in this period of life is very largely of the arteriosclerotic or senescent type. Accordingly the increased number of deaths is due, in great measure, to the aging of the population whereby more and more persons attain those higher ages where senile degeneration of the heart is the most common cause of death. This may be a by-product of the increase of the average duration of human life. The encouraging side of the picture is a marked declining tendency in the deathrate from the endocardial and valvular affections in early adult and middle life. These types of cardiac disease have their origin largely in acute rheumatism, syphilis, certain communicable diseases of childhood and focal infections. We may look forward to continued improvement as the result of the decline which is going on in the incidence of these controllable diseases.—*Bulletin Metropolitan Life Insurance Company.*

END-RESULTS IN EXOPHTHALMIC GOITER*

Patients Treated in Pre-Iodine Days

BY HELEN SINCLAIR PITTMAN, M.D.†

THE introduction of the therapeutic use of iodine has revolutionized the treatment of exophthalmic goiter. It has seemed worth while, therefore, to investigate the present condition of several patients who were treated for that disease before iodine was introduced. For the purpose of this study an attempt has been made to follow the records of 168 patients treated at the Massachusetts General Hospital prior to 1923, the year in which Plummer's[1] first article on the use of iodine in toxic goiter appeared. The patients comprising this group were unselected. They received their treatment between 1913 and 1923. The minimum follow-up period is, therefore, nine years. An effort has been made to trace all individuals treated during those years. All the 168 patients in this series were followed for a period of not less than six months after leaving the hospital, and most of them for at least two years. Hospital patients, however, in a city are usually those of a floating population and it is impossible at the present time to locate about half of them. Of the 168 patients treated in the years mentioned, 94 have been located. Of these; 20 have been unable to return to the hospital but have written of their condition, two have been reported from outside sources, 8 are dead and 64 returned. Each individual who returned had basal metabolic rate determinations and any special examinations (electrocardiogram, blood, urine and so forth) indicated.

There is thus information concerning 94 individuals, or 55 per cent of those treated.

Before the introduction of iodine, thyroid surgery in Graves' disease was not the simple matter which it is to-day. The operative mortality rate in Graves' disease at the Massachusetts General Hospital in the years 1909-1914[2] was 15 per cent. From 1920-1921 this had been brought down to three per cent.

There were three accepted modes of treatment:

1. X-ray alone: This was given to 61 patients, on 38 of whom there are recent data.
2. X-ray combined with surgery: This was employed in 35 patients, on 26 of whom there are recent data.
3. Surgery alone: This was practiced on 67 patients, on 30 of whom there are recent data.

In evaluating the status of the patients this year, I have grouped them according to the treatment which they received. Of the original series of 168 patients, five records have been destroyed, making the classification of treatment based on a series of 163 instances.

Group I, comprising 38 individuals, were treated by x-ray alone. Holmes[3] wrote in 1919 that it is possible to decrease the activity of the thyroid gland and probably to destroy its glandular structure by exposure to the Roentgen ray. Such treatment applied in cases of thyrotoxicosis produces relief of symptoms and shortens the course of the disease. He felt at that time that the Roentgen ray accompanied by rest should be tried in all cases of thyrotoxicosis and should be continued for a sufficient time to at least cause involution of the thymus, before resorting to surgery. The dangers of x-ray are less than those of surgery and in the milder cases it obviates the necessity of interfering with the daily life of the patient. If relief was not obtained after nine treatments, or if for any reason it was desirable to hasten the process, surgery might be recommended. The previous treatment by Roentgen rays will have been of benefit in reducing the operative risk by destroying the thymus gland. In a later article Holmes[4] gave as indications for operation, the failure to respond as indicated by a lowering of basal metabolic and pulse rates with corresponding gain in weight after six months of treatment. Means and Holmes[5] reported that about two-thirds of their cases treated by this method showed recovery or improvement. Read[6] has recently reported the present status of eight patients of a series of 36 treated prior to 1924, all of whom are now well. Hayes[7] found that of 100 consecutive, unselected, private patients treated by x-rays in the years 1911-1926, 62 per cent were cured in 1927. No individual in his series developed myxedema.

1. In the present series there are 38 instances of treatment by x-ray alone. Of these 26 are cured of their thyroid disease, four are dead, three have chronic mild hyperthyroidism, four are myxedematous but controlled, and one has a severe complication.

The last patient mentioned presents one of the most serious complications of hyperthyroidism. After eight treatments she was completely relieved of her thyrotoxicosis but had a severe residual exophthalmos which, because of corneal ulceration, ultimately required bilateral enucleation. This case was reported by Lahey[8].

2. Twenty-six individuals in the present series were treated by x-ray in conjunction with

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surgery; one is dead, 22 are well, and three have chronic mild hyperthyroidism.

Group III is made up of 30 individuals who were treated by surgery alone. This was, in those individuals who were toxic, a series of graded operations: ligation of one or both superior thyroid arteries, hemithyroidectomy or subtotal thyroidectomy. With patients prepared for operation by bedrest alone or combined with the administration of quinine hydrobromide, the operative risk was too great, in most instances, to allow of the single operation of sub-total thyroidectomy commonly employed at the present time. The single operation of choice was hemithyroidectomy. In 1920, Judd[9] obtained information from 88 individuals out of a series of 100 consecutive exophthalmic goiter patients on whom he had operated in 1914 (64 primary or secondary ligation, 36 primary thyroidectomy). Sixty-five and eight-tenths per cent were cured and 15 per cent had died from all causes during the six years. Hueck[10] was able to follow 54 patients of a series of 79 treated between 1912-1925 by surgery alone or by x-ray in addition to surgery and found that 78 per cent were able to do full work.

In our series, 30 individuals were treated by surgery alone. Of these, three are dead, 21 are well, two have chronic mild hyperthyroidism, three have myxedema, and one is in a state mental hospital with a major psychosis.

The results obtained in the three groups are compared in table I.

now, 15 years after her last radiation, presents the picture of chronic mild hyperthyroidism with a +20 per cent rate. Two other individuals (E. N. No. 48 and E. D. No. 316) were treated over a period of four years and are now well.

Of those treated by x-ray combined with surgery, 15 were given radiation before operation, five after, three both before and after, and in two individuals radiation was done following ligation of the thyroid arteries and before hemithyroidectomy. In this group the larger number (14) required from six months to a year for treatment, four completed their treatment in less than six months and one (M.G. No. 1382) was treated over a period of three years. In 1922 she had an initial rate of +40 per cent; a right lobectomy with removal of the isthmus was done in April of that year without affording her permanent relief. Four Roentgen ray treatments were given in 1924 but it was not until February, 1927 that her rate dropped to a normal level (—3 per cent). At the present time she is cured of her thyroid disease but at the age of 66 years she has arteriosclerotic heart disease with a blood pressure of 160/90.

Of the individuals treated by surgery alone, 19 had one operation (four subtotal and 15 hemithyroidectomies), five had two operations, five were operated upon three times and one (M. L. No. 326717) had five operations, the first in 1906, the last in 1913. At the present time she has a basal metabolic rate of +5 per cent with a pulse of 69. She gives evidence, however, of hypertensive heart disease with a blood pressure of 238/130.

TABLE I

Treatment	Original Series	Recent Reports	Well	Chronic Hyperthyroidism	Myxedema	Dead	Special
X-ray alone	61	38	26 (68%)	3	4	4	1
X-ray combined with surgery	35	26	22 (86%)	3	—	1	—
Surgery alone	67	30	21 (72%)	2	3	3	1
Records destroyed	5						
Totals	168	94	69 (73%)	8	7	8	2

THE RECORDS OF 168 CASES

Discussion: In the x-ray group 18 individuals received treatment for a period of between six months and one year. Two individuals received each one treatment only (I. C. No. 1649 and A. M. No. 1170); both are now well. One of the most striking points in the records of this series of individuals is the length of time required for some of them to attain a normal metabolic level after the beginning of treatment. A. L. No. 25 had an initial rate of +83 per cent in 1915 during which year she had seven x-ray treatments, and never became normal until 1922 when she had a rate of +4 per cent. At present she presents a cure with a rate of —4 per cent and at the age of 50 years has no evidence of cardiovascular disease. J. B. No. 68 received 29 treatments over a period of four years and

Summary and Conclusions: Recent data (64 examinations, 30 letters) are presented on 94 individuals out of a series of 168 patients treated for exophthalmic goiter between 1913 and 1923. These individuals were treated by one of three methods: x-ray, x-ray combined with surgery, or surgery alone. Sixty-nine (73 per cent) are well; eight have chronic mild hyperthyroidism; seven are myxedematous; one individual has had a bilateral enucleation for corneal ulceration secondary to a persistent severe exophthalmos; one is in a state mental hospital. The most satisfactory results have been obtained in the group treated by x-ray combined with surgery (86 per cent cures). In the groups treated by x-ray alone or surgery alone, there was very little dif-

ference, 68 per cent cures in the former and 72 per cent in the latter. The period required for relief of symptoms varied from a few weeks in two instances to a maximum period of seven years, with no consistent difference in the three groups in time required from beginning of treatment to cure. In the majority of individuals relief from symptoms was obtained in from six months to one year, a far longer time than is now usually required for cure by subtotal thyroidectomy in the iodinized patient. The methods employed in the years studied are shown to have given good results after a period of not less than nine years, but each method entailed a longer period of treatment than do present methods.

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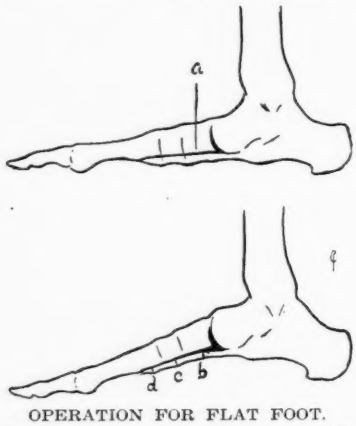
FLAT FOOT

An Anatomical Reconstruction

BY FREDERIC JAY COTTON, M.D.,* AND GORDON MACKAY MORRISON, M.D.*

THE vast majority of flat feet call for no operation.

Many flat feet involve bony change; these cannot be "reconstructed" in any literal sense; must be operated on if need be by wedge operations, etc. But in others in which in Brackett's phrase "the bony architecture is unchanged" one can reconstruct. Among these is a type often seen in young men in which a long lax foot, pronated flat, shows perfectly evident relaxation of ligaments not presaging much chance of correction by exercise. Only in such cases is this operation to be considered. It rests on the fact that the weight is transmitted from the top of the astragalus through its downward rotated head to the supporting calcaneo-scaphoid ligament, a very definite and very strong structure even when relaxed. The operation consists in transferring the scaphoid attachment of the ligament farther forward so as to tighten up the ligamentous support. The technique is shown in the accompanying cut.



OPERATION FOR FLAT FOOT.

Upper figure: Shows the open astragalo-scaphoid joint—the cut (a) above the supporting ligament, carried forward across bones and articulations.

Lower figure: The foot corrected: the bone-ligament flap carried forward. The rear end of the scaphoid in the graft (b), the scapho-cuneiform articulation (c), the cuneiform-metatarsal (d) are all carried forward one-half inch—and the whole strip pegged in place.

The astragalo-scaphoid joint is opened and a rather broad, thin osteotome, pointing outward and about 35 degrees downward, is driven through to the plantar surface of the bone, separating (roughly) one quarter of the scaphoid.

The line of the cut is continued forward, disregarding joint intervals, to ¾ inch in front of the base of the first metatarsal.

If then the foot is corrected into proper position in the direction of cavo-varus, then the bony flap, containing parts of scaphoid, of internal cuneiform and of metatarsal base, is easily slid forward to a new hold. The bony flap is loosened, never dug out of its bed on the under side.

The front end, the metatarsal piece, may be trimmed off as superfluous, and the main flap is to be pinned in its new place with small ivory or bone pegs.

CASE:

J. D. (man now 27 years old), operated on at the Boston City Hospital in 1920, was examined in July, 1933. One foot only had been operated on (with expectation of doing the other after an interval). Thirteen years after, it showed a foot perfectly normal in stance and mobility. The left foot still showed a lax flat foot of extreme type with troublesome weakness.

In a very few other cases treated the result was good, but none other followed up for a long time.

The operation in no way interferes with lateral rotary motion in the subastragaloid joint.

The only drawback is the need of waiting for solid bony union before unrestricted unsupported weight-bearing is resumed.

This operation is applicable to only a small selected group of cases; it is only one of many corrective measures for the relief of flat foot.

*For records and addresses of authors see page 817, issue of April 12, 1934.

INTERN TRAINING IN MASSACHUSETTS*

By the Committee on Medical Education and Medical Diplomas of the Massachusetts Medical Society†

IN this country it is generally agreed that one of the most significant phases of medical education is that which has to do with the training of hospital interns and that the future progress of medicine depends in no small degree upon the way in which these interns are trained. During 1933, more than 5000 medical school pupils received postgraduate education as interns in our various hospitals: in New England, alone, 510 interns were at work in the fifty-nine hospitals approved by the American Medical Association to offer such training.

The Committee on Medical Education and Medical Diplomas of the Massachusetts Medical Society, recognizing the importance of internships to medical progress, has considered it desirable to make a preliminary survey of the internships available in this state in order to ascertain, if possible, how our internships are filled; whether they are good, bad, or indifferent and whether any suggestions can be offered to make them more valuable. The results of this survey are reported here.

MASSACHUSETTS INTERNS

Thirty-one Massachusetts hospitals are approved by the American Medical Association for intern training and help to educate each year a group of 312 doctors. During 1933, these doctors assembled from far and wide, but were mostly graduates as might be expected, of Tufts, Harvard and Boston University. In addition, thirty-six other American Medical Colleges, two Canadian and three foreign schools, sent pupils to be trained here. Two hospitals have attempted an experiment of very questionable usefulness by receiving as interns doctors from unrecognized medical schools.

The interns of 1933, presumably, were a typical group. On the whole, they were recent graduates, migrating as quickly as possible from the shelter of their various schools, to the broader experience of hospital life. One man who graduated in 1925, received an appointment. He was by far the oldest man on the list, he had come to us from the West and was taking this means to obtain in Boston the postgraduate training in surgery that he felt he needed.

Five of our hospitals claim not to discourage the appointment of women interns. In spite of this, but ten women interns were enrolled. This fact perhaps deserves comment since nowadays nearly five per cent of all medical students graduating each year are women. A fair annual quota of women for Massachusetts to enroll as interns would be nearer fifteen than ten. Good women students can be used very advantageously and should be given better opportunity.

If the 312 Massachusetts interns are regarded as a class, it is interesting to note how this class is made up scholastically. Half of these students graduated in the upper third of the medical schools whence they came, and only a fifth in the lower third. Thus Massachusetts cannot complain of the intellectual abilities of her interns.

MASSACHUSETTS INTERNSHIPS

The quality of the Massachusetts internships which are available is a more difficult matter to analyze. In general, internships are of three types: The straight "medical" or "surgical," the "rotating" and the "special service" internship. They vary in length from one to two or more years' duration and are designed to offer intensive postgraduate instruction. "Rotating" services are much more frequently offered than the straight "medical", or "surgical" and are planned to give the student a bird's-eye view of his profession. The typical "rotating" service, for example, is too short. In two years' time or less it attempts to include a period of work in surgery, medicine, obstetrics, eye, ear, nose and throat diseases, and often in neurology, pediatrics and dermatology as well. The straight "medical", "surgical", or "special" services offer in about the same time interval a period of more concentrated training in one or the other more general or special branches of the profession.

Many factors play a part in determining good or mediocre internships. One very striking feature is the great variability in the number of hospital beds per intern. Several hospitals are understaffed and expect their interns to cover more than fifty beds per man; while at the other end of the list are two so arranged that they have an intern for each eleven beds. It seems fair to assume that no intern can cover satisfactorily more than about thirty beds; if he is asked to do more than this he cannot receive a very good training.

In order to show certain of the most noteworthy differences between hospitals which attract good and mediocre intern material, comparative data have been tabulated from four hospitals of somewhat similar size, the first two affording the best type of medical or surgical training,

*Presented before the New England Hospital Association at Boston, February 17, 1934.

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and the other two a "rotating" training less valuable.

It is evident, on the whole, that the better scholars—and by and large they make the better interns—tend to concentrate in comfortably endowed hospitals where there is a resident staff large enough to carry forward a satisfactory type of clinical work, and in institutions where the percentage of necropsies is high. This figure has come to be generally recognized as a fair index of the educational activities of a hospital.

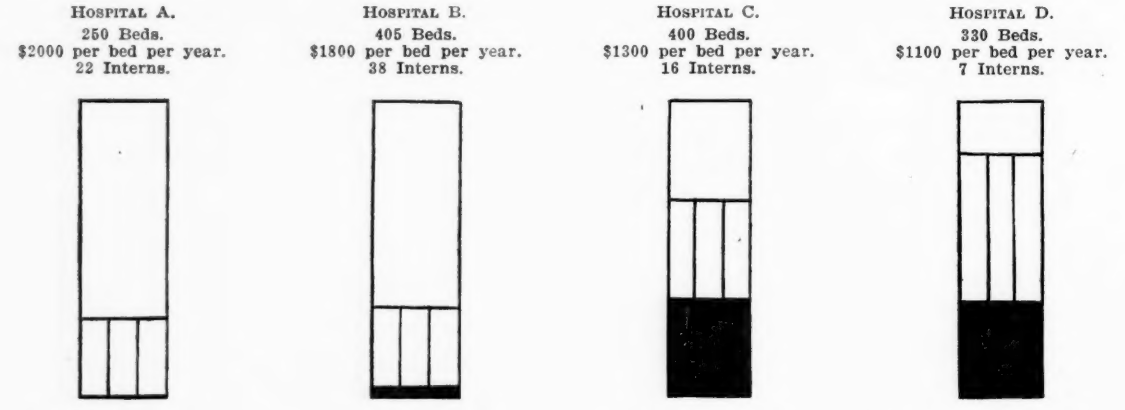

FIGURE 1.

Interns of four hospitals. The plain column is proportion of interns in first third of their class; the solid column lowest third, and the broken column middle third.

HOW TO IMPROVE MASSACHUSETTS INTERNSHIPS

Massachusetts is in a position to improve her internships. There are many well-equipped hospitals, and excellent intern material is at hand each year. The problem is to develop these hospitals as centers of postgraduate education to better advantage, and to improve their general average of intern training.

Each hospital which has placed itself on record as being capable of training interns must recognize that in so doing it has assumed all the responsibilities of a Teaching Hospital. The Staff, Trustees, and Superintendent must admit this fact and must coöperate to improve the opportunities for their house-pupils to receive adequate and proper instructional facilities.

No intern should be appointed who is not a graduate of a medical college recognized by the Massachusetts Medical Society. No intern should be appointed without a personal interview and preferably should receive some sort of an examination regarding his abilities before he is accepted. The intern's quarters should be attractive, his food good, and he should have adequate facilities for rest, privacy, study and recreation. It has been pointed out that in one Massachusetts Hospital about a third of the interns enter the institution as patients at some time during their period of service. The amount of intra-mural illness should be kept as low as possible and this can only be accomplished by proper care of the personnel.

The Council on Hospitals and Medical Education of the American Medical Association approves of a "rotating" internship as an essential for a hospital to be approved for intern training. If young doctors are best initiated into practice by this kind of hospital experience, "rotating" internships must be made more desirable. At present, in Massachusetts, they are not greatly sought after. An appreciably poorer type of student is trained in hospitals offering this kind of internship than in those offering only "medical" or "surgical" services. In order to improve this state of affairs, the teaching in these hospitals must be conducted with especial care.

THE HOSPITAL AS A TEACHING CENTER

Staff, Trustees and Superintendents of hospitals with "rotating" interns should work together more purposefully to organize the best possible kind of intern teaching. For example, in every hospital a carefully considered and well-planned intern curriculum should be developed by an appropriate committee; certain staff members, especially if they have a bent for teaching, should be delegated to see to it that the intern's work is checked up; that his records are up-to-date and well and carefully written, that his routine laboratory and clinical work is properly done, that his physical examinations as recorded are accurate, that diagnoses are made correctly and that treatment is carried out properly and systematically. A visit with the intern should be made each day to each of the intern's patients by a competent member of the Visiting Staff, unhurriedly and as a

teacher, so that everything the intern does can be scrutinized and criticized. The number of necropsies should be increased, interns and visiting staff doing all in their power to study diagnosis and treatment by the method of clinical-pathological correlation. In too many hospitals the intern's work is haphazard and superficial. The self-taught intern does not acquire much useful knowledge; he needs to be drilled in the art of practice, an art that can only be mastered by hard work intelligently controlled.

The intern should be encouraged to grow and develop. He should be urged to take an active part in staff conferences and in other medical meetings held under the hospital's auspices. Hospitals and staff meetings should be conducted regularly and with a certain degree of formality. They should be run off on time and the intern should present the cases under discussion, learning to speak on his feet, without notes, and clearly and succinctly. Too often, at such meetings, the intern is made to sit on the side lines and do the listening. This is discouraging, especially, as almost invariably, with a little coaching, he can learn to give a good account of himself.

Hospital Trustees must be educated to realize that a Teaching Hospital requires certain equipment in addition to first-rate wards, laboratories and operating rooms. There must be an enthusiastic, well-selected staff acting under good leadership. There must be a sufficient number of interns in proportion to the number of beds so that each intern may have a chance to think and work at something out of his routine. There must be a suitable place for medical meetings and this room should contain apparatus for demonstrating charts, x-ray films or pathological specimens. There must be a library in the hospital, readily accessible to the interns and staff, and it should receive sufficient endowment to enable it to purchase up-to-date textbooks, as they are published, and to subscribe to the more useful medical journals.

The intern should be encouraged to write. Medical writing, if it does nothing else, stimulates a beginner to wish to use a library properly, teaches him to read, analyze, criticize or abstract literature, and also something of facility of expression and of the difficulties of composition—all good things for a young doctor's development. The Allegheny County Medical Society of Pennsylvania has initiated an important experiment along this line by offering an annual prize of $50 for the best case report submitted by interns of any approved hospital in the County. It would be a fine stimulus if the Massachusetts Medical Society were to offer a similar prize each year for the best case report written by an intern holding any of the Massachusetts rotating appointments. The chance to win such a prize might prove very inspiring.

The difference between good and bad intern training is not easy to analyze, since so much depends upon personalities. One fact, however, is very clear. The pace at which a hospital works and the quality of what it accomplishes depend on coöperation of the Staff, Trustees and Superintendent. These three bodies must understand each other's problems and must act in harmony. To admit that a hospital which trains interns is a Teaching Hospital, is a long step forward, for a Teaching Hospital has certain ideals and responsibilities which differentiate it sharply from an institution in which there is no teaching. The best organization of a Teaching Hospital differs in each community and requires careful consideration. Certainly no single plan of organization can be generally successful. The quality of the interns of Massachusetts can be improved and they can be given better training if the staffs, trustees and superintendents of our hospitals are interested to improve the medical education of interns and are willing to take an active part in advancing this aspect of their hospital's functions.

MORTALITY RATES

Telegraphic returns from 86 cities, with a total population of thirty-seven millions for the week ending April 7, indicate a mortality rate of 12.6 as against a rate of 11.6 for the corresponding week of last year. The highest rate (20.1) appears for Trenton, N. J., and Wilmington, Del., and the lowest (3.6) for Yonkers, N. Y. The highest infant mortality rate (16.1) appears for Duluth, Minn., and the lowest for Bridgeport, Conn., Knoxville, Tenn., Lynn, Mass., Somerville, Mass., South Bend, Ind., and Yonkers, N. Y., which reported no infant mortality.

The annual rate for 86 cities is 12.7 for the fourteen weeks of 1934 as against a rate of 12.2 for the corresponding period of the previous year.

SUMMARY OF DEATHS AND DEATH RATES (ANNUAL BASIS) FROM AUTOMOBILE ACCIDENTS PER 100,000 ESTIMATED POPULATION FOR 86 CITIES FOR CORRESPONDING PERIODS OF 1934 AND 1933.

	Week ending		First 14 Weeks	
	April 7 1934	April 8 1933	1934	1933
Total deaths	173	138	2,227	1,962
Deathrate	24.1	19.2	22.2	19.5

CASE RECORDS
of the
MASSACHUSETTS GENERAL HOSPITAL

ANTE MORTEM AND POST MORTEM RECORDS AS USED IN WEEKLY CLINICAL-PATHOLOGIC EXERCISES

EDITED BY RICHARD C. CABOT, M.D.
F. M. PAINTER, A.B., ASSISTANT EDITOR

CASE 20171

PRESENTATION OF CASE

This is the case of a forty-two year old American.

Three weeks before admission while talking with a friend everything became dark and he thought he was going to faint. At the same time he had severe pain in the back of his neck and the left side of his head. Following the attack this pain was present intermittently until admission. For a few days after the onset of the pain he also complained of stiffness of his neck and of the calves of his legs. He was told by his doctor that he had a blood pressure of 230. The patient refused hospitalization at that time. He remained at home most of the time, was very apprehensive, and insisted that his wife be with him all the time. He complained of peculiar feelings and noises in his head. On the morning of admission he informed his wife that he was about to take an enema. Some time later she heard him call to her from the bathroom. She was sure that he did not fall down because she was in the next room and had heard no noise. When the patient was found he was lying on the floor unconscious, his body limp and his eyes set. A physician gave him a stimulant which revived him for a while. He then became very noisy and violent, but was finally quieted with a sedative. There is no history of any visual disturbance, fever, cough or pain in the chest during the three weeks preceding admission.

His mother died of cancer of the uterus, his father of angina. Two sisters were living and well. A third had died of pulmonary tuberculosis.

He had been married eighteen years. His wife and two children were living and well. There had been no miscarriages.

Ten years before admission he had been at a hospital where a diagnosis of gastric or duodenal ulcer was made. Operation was advised but was refused. Four years before admission at another hospital a diagnosis of gastric ulcer was made. He was put on a diet, but did not adhere to it very conscientiously. He had no severe bleeding.

Physical examination showed a thin semistuporous man. The left pupil was oval in shape. Both fundi showed redness and hazy disks. There was slight choking of the disks, probably one diopter, and slight nicking of the veins, with some tortuosity of the vessels. There was some stiffness of the neck, not marked. The heart was not enlarged. The blood pressure was 202/120. When a Kernig test was attempted he complained of pain in his hamstrings. He was clear mentally, but his memory for recent events was poor. He was quite irritable and very noisy. He had difficulty in choosing words and sometimes used the wrong word to express himself. There were no uncinate attacks. Examination of all his cranial nerves was negative. His reflexes were all active on both sides. There was a slightly positive Kernig on both sides. The biceps, triceps and knee jerks were slightly hyperactive. The Babinski was negative, but from his history it was said to have been positive on both sides one week before entry.

The temperature was 98.8°, the pulse 52, the respiratory rate 11.

Examination of the urine was negative. Examination of the blood showed a red cell count of 4,800,000. The hemoglobin was 75 per cent. The white cell count was 15,500, with 82 per cent polymorphonuclears. A Hinton test on the blood was negative. The blood sugar was 98 milligrams, the non-protein nitrogen 29.

A lumbar puncture showed grossly bloody fluid. Pulse and respiratory oscillations were normal. The initial pressure was 300; after removal of 5 cubic centimeters of fluid it went down very slowly to 245. The cell count showed 1,500,000 red blood cells and 1200 white blood cells. The fluid was xanthochromic in the centrifuged specimen. The Wassermann was negative. A second lumbar puncture done three days after the first showed grossly bloody fluid and an initial pressure of 120. About 8 cubic centimeters of fluid was removed, at which time the pressure was 60. A cell count showed 62,000 red blood cells and 600 white blood cells. The centrifuged specimen was definitely xanthochromic. The total protein was 126, the sugar 38.2, and the colloidal gold 1112222100. A third lumbar puncture done three days later showed cloudy yellow fluid. The initial pressure was 280. After the removal of 16 cubic centimeters the pressure went down to 140. The cell count showed 1760 crenated red blood cells, 320 polymorphonuclears and 320 lymphocytes. An alcohol test was positive. The ammonium sulphate test was negative. The total protein was 101, the colloidal gold 0122210000. The centrifuged specimen showed a scanty red sediment with xanthochromic fluid above.

On his twelfth day in this hospital the patient suddenly cried out, complained of pain behind his left eye and lapsed into stupor. Examination showed stiffness of the left arm and leg and flaccidity on the right. The deep reflexes were symmetrical but very weak. Bilateral Babinski was present. The blood pressure, which had been about 180/120, was now

230/150. He remained in a semistuporous condition throughout that day, groaning continually. On the following day however he was quite comfortable and quiet and was even allowed one cigarette. His mind was clear.

The day after this upon his request he was given a bedpan. Five minutes later he was found breathing noisily, with his right eye closed, a blood pressure of about 125/100 and a very weak pulse. He could not be aroused. All his limbs were flaccid, but reflexes were obtained on both sides. About fifteen minutes later he became very cyanotic and in spite of artificial respiration died.

Differential Diagnosis

Dr. Tracy J. Putnam: A man who is substantially healthy has two acute episodes, one mild one, followed in three weeks' time by one which renders him unconscious. I think our first thought on hearing the history to that extent is that the patient has had a cerebrovascular accident of some kind. Perhaps the first thing to think of is that he had a thrombosis which later gave rise to a hemorrhage, a thing which we know often happens, although I think the three week interval is rather unusually long. As we look over the precise symptoms that he had, however, that possibility becomes somewhat less probable and I think we can find a good many manifestations that can be explained better on a basis of subarachnoid hemorrhage than of hemorrhage within the cerebral substance. In the first place pain in the back of the neck and headache are rather unusual with thrombosis. That is apt to come on painlessly. Another thing is the blood pressure. We expect the blood pressure to come down following thrombosis or hemorrhage within the cerebral substance. The mental perturbation is perhaps not very specific of one thing or another.

Of course the onset of an accident in the bathroom is a very common manifestation.

I think the past history adds nothing, at least the findings are not very germane to the situation here. Nor is the neurologic examination very important, except that there are mild signs of meningeal involvement, specifically the difficulty in carrying out the Kernig test.

I should like to call attention again to the persistent high blood pressure, which would certainly be unusual if this were the ordinary type of cerebral hemorrhage. So is the spinal fluid when we come to that. The fluid was grossly bloody, with an initial pressure of 300 and over a million and a half red cells. That is an extremely bloody fluid of course, almost one third pure blood. It would be very unusual for a man to have a massive hemorrhage deep in the substance of the brain and have enough of this hemorrhage leak into the spinal fluid to give him such a high cell count and for him to survive as long as this patient did. Moreover, on centrifuging the fluid was seen to be xanthochromic, which is definite evidence of course that the hemorrhage has existed for some time. That raises the presumption that it came on three weeks earlier. I should like to call your attention to the fact that there were twelve hundred white cells, which again is evidence of long-continued irritation of the meninges from the presence of red cells in the fluid.

The pressure apparently came down and so did the count of red cells, although the number of white cells increased. This is what we should expect with a gradually improving subarachnoid hemorrhage.

An interesting point is that we do not expect to find arteriosclerosis as an etiological factor in the ordinary type of subarachnoid hemorrhage. Subarachnoid hemorrhage by and large is a disease of young people rather than of arteriosclerotic people. I do not suppose, however, that the presence of arteriosclerosis will prevent subarachnoid hemorrhage, and it is quite possible that this patient has a congenital aneurysm, which is the ordinary cause in addition to arteriosclerosis.

The terminal event I think is quite obviously a recurrence of the original hemorrhage, and once more it comes on with pain. The neurologic findings are not adequate, it seems to me, to permit us to localize the site of origin of this hemorrhage. The record is rather noncommittal on this occasion, although of course we know from experience that aneurysms are most apt to be in the circle of Willis or one of its branches. Perhaps if we wanted to be very accurate about it we might say that the pain behind the left eye suggests that the aneurysm was on the left and that the pain was due to pressure on the sensitive meninges about the sinuses. On the other hand it is a little hard to explain why his right eye should be closed under these circumstances at a later attack.

To sum up, this man obviously has arteriosclerosis with a high blood pressure, and we should expect to find evidence of that in the brain. He also evidently has a subarachnoid hemorrhage. It is difficult to be sure that he has not a certain amount of intracerebral hemorrhage, but that seems unlikely. It seems more probable that he has a combination of congenital aneurysm with arteriosclerosis.

Clinical Diagnosis

Subarachnoid hemorrhage.

Anatomic Diagnoses

Subarachnoid hemorrhage.
Ruptured aneurysm of anterior communicating artery.
Probable rupture of left middle cerebral artery.
Duodenal ulcer, perforated.

General peritonitis.
Emphysema, bilateral apical.
Cervical rib, bilateral.
Arteriosclerosis.

Pathologic Discussion

Dr. Tracy B. Mallory: The autopsy on this man showed outside the head two entirely unexpected findings. The final attack of coma and death may in fact have had nothing whatever to do with his cerebral pathology. You remember that far back in the past history he had had a diagnosis of ulcer of the stomach. That ulcer turned out to be in the duodenum rather than the stomach. It had perforated and he had a general peritonitis. That is of some interest in connection with Dr. Cushing's theory of the activation of stomach ulcers by certain brain lesions.

The other rather unusual finding of absolutely no significance in his illness was a bilateral emphysema of both apices of the lungs. This was very sharply localized, just at the apices, and on examining the thoracic cavity it was evident that the apices of the thoracic cavity were unusually high, probably due to bilateral cervical ribs. I made this cast of it. He had approximately three times as much lung above his clavicle as the average person, and the emphysema on each side was absolutely localized to that area. The bronchi leading to these areas were normal or slightly dilated, certainly not obstructed. The remainder of the lungs showed no emphysema whatever.

The cerebral findings come much closer to Dr. Putnam's prediction.

Dr. Charles S. Kubik: On examination, the brain showed only a moderate amount of blood in the subarachnoid space. On the inferior surface of the optic chiasm there was a mass one centimeter in diameter consisting of partly organized clotted blood which obviously had come from a ruptured aneurysm of the anterior communicating artery. This was a thin-walled affair about two millimeters in diameter. No aneurysms of any of the other cerebral arteries were found. There was a moderate degree of arteriosclerosis.

Aneurysms such as this, in or near the circle of Willis, are found in most cases of spontaneous subarachnoid hemorrhage. The subjects are usually young people without arteriosclerosis or hypertension and without history or other evidences of syphilis. The aneurysms, or a majority of them, are probably the result of a congenital defect in the muscularis. It is thought that infected emboli coming from an endocarditis may account for some of them. In the case before us the wall of the aneurysm was not sclerotic, and I should suppose that here too there was probably congenital weakness of the vessel wall, with hypertension as an additional factor.

Dr. Mallory: I neglected to mention that throughout the body there was a diffuse arteriolar sclerosis, which one would expect with a long-standing hypertension.

CASE 20172

Presentation of Case

A forty-three year old French weaver entered complaining of pain in his chest of three weeks' duration.

A year and a half before admission he first noticed dyspnea and cough, worse on exertion. The dyspnea disappeared after a few weeks, but the cough still dragged on. He was comparatively well until three weeks before admission, when marked dyspnea on exertion appeared again. This was associated with cough and blood-stained sputum. He had one or two sharp attacks of orthopnea. He had to sleep on two pillows. He also experienced a dull aching substernal pain, aggravated by exercise. One week before admission he noticed swelling of his abdomen.

His family and marital histories are irrelevant.

Two months and a half before entry he had all his teeth removed.

Physical examination showed a well-developed and nourished man propped up in bed. There was slight cyanosis of the lips. His chest was barrel shaped. The heart was markedly enlarged to the left, measuring 11.5 centimeters from the midsternal line in the fifth interspace. The supracardiac dullness measured six centimeters. The pulse was small, thready, and almost impossible to feel. The blood pressure was 155/130. There were râles at both bases. The liver edge was sharp, smooth, tender, and palpable four fingerbreadths below the costal margin. There was a large right scrotal hernia and a healed herniotomy scar on the left. There was slight fullness of the flanks with questionable shifting dullness and questionable fluid wave.

The temperature was 98.6°, the pulse 100. The respirations were 20.

Examination of the urine showed a specific gravity of 1.010 to 1.022 and a slight trace of albumin. The sediment showed occasional hyalin casts and a rare white blood cell. Examination of the blood showed a red cell count of 5,680,000 and a hemoglobin of 70 per cent. The white cell count was 8500, with 70 per cent polymorphonuclears. The stools were negative. Hinton and Wassermann tests were negative. The non-protein nitrogen was 33 milligrams. A phenolsulphonephthalein test showed 68 per cent secretion at the end of one hour, 33 per cent of which was excreted in the first fifteen minutes.

An electrocardiogram showed normal rhythm, rate 105, slightly widened Q R S waves, flat T_1 and T_2, and slight left axis deviation.

X-ray examination of the heart showed enlargement, the transverse diameter measuring 18.3 centimeters, 15 to the left and 3.3 to the right. The transverse diameter of the chest measured 30 centimeters. There was marked prominence of the left ventricle. The supracardiac shadow was considerably increased in the anteroposterior view. In the lateral view however the aorta appeared of normal size.

He was put on digitalis and got good diuresis. Nine days after admission his temperature rose to 103.2° and that evening to 104°. There was questionable slight dullness at the right base. He showed slight anorexia and the digitalis was omitted. The following day there were many dull moist râles at the right base, with coarse moist rhonchi. The sputum that morning was rusty and pneumococcus type II was obtained from it. X-ray examination of the chest at this time showed extensive mottled dullness involving the lower two thirds of the right lung field. The dullness was more intense in the midportion of the chest. The upper portion of the right lung field and the entire left lung field were clear. The patient two beds away had a type II pneumonia and it was believed that a cross infection had occurred. Two days after the onset of the rise in temperature he was given serum after a negative eye test and a questionable skin test. The first 5 cubic centimeters was given without reaction, but after 7 cubic centimeters of the 25 cubic centimeter dose was injected he felt weak and began to sweat, his pulse became poor and his blood pressure went down to 70/50. The injection was stopped. After ten drops of adrenalin his blood pressure rose to 130/90. He was desensitized without any reaction. He became slightly cyanotic and was put into an oxygen tent. His temperature remained elevated, reaching 104.2°. The day following the serum treatment his pulse became rather small, rate 140, and he was moderately cyanotic. His white blood cell count, which had been 20,900 at the onset of the pneumonia, dropped to 4,000. His blood pressure steadily failed and he died that day, three days after the onset of the pneumonia.

Differential Diagnosis

Dr. F. Dennette Adams: The history is one of cardiac failure of the congestive type beginning three years before the final break and gradually becoming worse. The cough was doubtless due to mild congestion of the lungs.

There are these possible etiologic factors: rheumatic, syphilitic, and hypertensive-arteriosclerotic heart disease. There is nothing in the history pointing toward a rheumatic background and no murmurs are mentioned in the physical examination, so rheumatic disease can readily be excluded.

The cardiac break began at forty, which is within the age zone of syphilitic heart failure. Against the likelihood of this disease, however, is the interval of three years between the onset of the first symptoms and of the final break. The characteristic murmurs are also absent. The x-ray observation of widening of the arch would suggest syphilis, but the normal appearance in the lateral plate offsets the evidence obtained by the anteroposterior view.

The man had hypertension before he came into the hospital, with a pressure doubtless higher than the reading of 155/130 recorded at the time of admission, which was after the failure had become well advanced. It is safe to assume that we are dealing primarily with a case of hypertensive heart disease with failure.

Whether angina pectoris, coronary disease, or coronary occlusion was present it is impossible to determine from the facts given in the history. The chief complaint is recorded as pain in the chest of three weeks' duration, but the account given in the history of the present illness stresses shortness of breath and also a dull aching substernal pain aggravated by exercise. It is important to know more about the pain, its degree, type and character of onset, before any conclusions concerning coronary disease can justifiably be drawn.

The electrocardiogram in this instance is of little help. An electrocardiogram showing a low T wave, if taken shortly after admission, might point toward coronary change; but if taken two or three days later and presumably following digitalis therapy, the low or flattened T wave loses its value as a diagnostic aid.

Certainly the kidneys are not appreciably involved.

The abdominal swelling makes one suspicious of moderate ascites. Apparently the physician who performed the physical examination suspected the possibility of its presence, but the evidence is not convincing. It is likely that the feeling of distention of which the patient complained was caused by congestion of the liver, occurring fairly suddenly along with the other manifestations of the acute break. I do not believe that ascites is present.

The barrel chest suggests emphysema. Nothing is recorded about lung signs and nothing reported in the x-ray about emphysema. There is one other fact which also points toward this possibility, namely, that the left side of the heart and the width of the arch were found greater by x-ray than by percussion. These are rather indirect bits of evidence, but of some significance nevertheless.

The acute infection must have been pneumonia, doubtless a cross infection from the other patient. We know that such occurrences are not rare. Here we have a splendid example of the need for isolation of pneumonia patients, an ideal procedure difficult to carry out in any general hospital. Bronchopneumonia is rare with type I or II pneumococcus, lobar pneumonia almost a certainty. The mottling seen by

x-ray is not at all inconsistent with the early stages. Whether he had involvement of the lower lobe or of the lower and middle lobes is difficult to decide. The fact that the greatest density by x-ray was in midchest points toward middle lobe rather than lower lobe, although nothing is recorded concerning the straight, clean-cut line which is usually seen by x-ray with middle lobe consolidation.

I admire the courage but question the wisdom of those who continued to give serum after they had encountered trouble once. I have no desire to appear too critical or too much of a reactionary, but I think I am justified in making the statement that type II serum has by no means been universally accepted as a therapeutic agent of proved merit, and that discontinuance of its administration after one severe serum reaction might have been a wiser course. We do not know that such a serum reaction does not have a detrimental effect on the patient in spite of recovery from the immediate symptoms. On the other hand, there are two sides to the problem, and those who have faith in the efficacy of type II serum therapy are justified in using it. Had the pneumonia been of type I origin the problem would have been different, for type I serum administered early is generally accepted as a therapeutic agent of some value. But it is none the less my conviction that some of the enthusiasm for serum therapy is not justified by any results which have thus far been demonstrated in connection with its use, and that its disadvantages are being minimized while its advantages are sometimes overstressed.

I should be interested to know if the patient had a positive blood culture. I always expect it in a sick pneumonia patient with a low white cell count.

DR. TRACY B. MALLORY: There were no positive cultures during life.

DR. ADAMS: My diagnoses in this case are:

Hypertensive and arteriosclerotic heart disease with congestive failure.

Possible coronary disease.

Lobar pneumonia of the right lower lobe, possibly of the right middle lobe.

Possible pneumococcus septicemia.

CLINICAL DISCUSSION

DR. FREDERICK T. LORD: There seems little question in respect to the nature of his pneumonic process, and I would agree that the finding of type II in the sputum in a patient with a complex of symptoms consistent with pneumonia is almost certain evidence of lobar pneumonia.

With respect to contagion, in Smillie's epidemiologic studies he finds that Types I and II pneumococci occur in family contacts in a percentage of about twenty per cent, but it is by no means certain how pneumonia arises under such circumstances. The frequency with which lobar pneumonia is preceded by a "cold" is perhaps significant in this connection, and it may be that there is a relationship between the filtrable virus concerned in the etiology of the "cold" and the pneumococci which cause pneumonia. Dochez's studies on the acute infections of the respiratory tract suggest that the filtrable virus which initiates the primary infection promotes secondary bacterial infection and the spread of the secondary invaders to contacts. In Smillie's studies contact alone does not seem an adequate explanation and the large proportion of those suffering from acute "colds" among carriers of homologous pneumococci in family contacts suggests that family epidemics of "colds" may determine the transfer of types I and II pneumococci from infected to uninfected individuals.

Smillie's findings suggest that there is little danger of contagion among patients or the staff in hospitals. The incidence of homologous pneumococci among contacts in hospitals is about two per cent in contrast to about twenty per cent in family contacts. The presence of a patient with type II pneumococcus pneumonia two beds away from this patient is hardly enough to prove contagion from one to the other, although, of course, one cannot deny it.

There is one aspect of this case especially deserving of comment, and that is that the pneumonia developed under observation in the hospital, and this affords an unusual opportunity to note the behavior of the temperature. In a few instances in which a type I or type II pneumococcus pneumonia has developed under such circumstances there has been a very rapid elevation of temperature from normal to its fastigium within the space of only a few hours, and in this patient the temperature rose from normal to 103° within a period of about four hours. In addition, the patient had a cough and bloody sputum, but the initial manifestations were atypical in the absence of chill and stitch in the side. An explosive onset and the grouping of initial symptoms are usually sufficient to suggest lobar pneumonia, but atypical features here and the presence of cardiac disease probably made the early diagnosis uncertain. An unusual opportunity is, of course, afforded for early treatment under these circumstances, and yet the diagnosis of type was not made until the day after the onset and serum was not given until the following day. This seems an unjustifiable delay if we plan to treat type II pneumococcus pneumonia with serum.

Another aspect of this problem is the result of the tests for hypersensitiveness to horse serum. The ophthalmic test was negative, but on the application of the intradermal skin test there was a wheal one centimeter in diameter without surrounding erythema. The introduction of 0.02 cc. of a 1:10 dilution of normal horse serum into the skin produces a white elevation only a few millimeters in diameter. If a

larger volume than 0.02 cc. is introduced the initial elevation is, of course, correspondingly larger. In judging the test, it is important to note the behavior of the inoculated region at frequent intervals and to regard as a positive reaction the rapid transformation of the small white elevation into a genuine urticarial wheal with a surrounding zone of erythema. The result of the skin test in this patient is probably negative.

The results of the skin test with normal horse serum diluted 1:10 with normal saline are difficult to judge on account of the occurrence of doubtful reactions and this difficulty is enhanced with Felton's antibody diluted 1:10 with 1.5 per cent salt solution. Confusing results with skin tests have led to the substitution of the less delicate ophthalmic test, but it is undesirable, I think, to abandon the skin test entirely and it is well for us to continue to use it here as an additional safeguard in connection with the history and the ophthalmic test.

Patients with obviously positive skin tests should not, I think, be treated with antipneumococcic serum. In patients with histories negative for hypersensitiveness and negative ophthalmic tests, but with doubtful skin tests, it is safer to proceed cautiously, starting with very small doses subcutaneously, i.e., from 0.005 to 0.025 cc., and doubling the dose every half hour until 1.0 cc. is given. Following this, 0.1 cc. diluted with normal saline may be given intravenously and the intravenous dose doubled every half hour until the required amount is given.

It is stated that the patient had sweating, weakness and low blood pressure after the injection of serum. In our experience about ten per cent of serum-treated patients have had a transient complex of symptoms, usually immediately after the first dose, including some shortness of breath, cyanosis, rapidity of the pulse, thoracic oppression and apprehension, and I would not regard the reaction this patient had as dangerous. It is not unusual to have a low blood pressure at the inception of a severe acute infection. I myself, when I had lobar pneumonia, had a blood pressure of 90/60 for the first twenty-four to thirty-six hours. It is not necessary to stop the use of serum under these circumstances. The subsequent injection of 45.0 cc. without trouble in this patient supports this point of view.

With respect to the merits of antipneumococcus serum in the treatment of type II pneumococcus pneumonia, analysis of the available evidence indicates that the usual mortality of type II is about 40 per cent and that serum has reduced the mortality to 30 per cent, and in early treated patients it is fair to assume that that mortality might be reduced to below 30 per cent. In the State project there have been eighty-four patients treated within the first four days of the illness with twenty-four deaths, a mortality of twenty-nine per cent.

DR. PAUL D. WHITE: I think that Dr. Adams has covered very well the cardiac side of the case and the rest of it too. The difficulty of determining clearly whether there was coronary disease from the history given is great. One would want a much more adequate story than Dr. Adams had to work on.

DR. MALLORY: Do you think the presence of cardiac decompensation influenced the reaction to the serum in any way?

DR. WHITE: I do not know. I suppose that anyone who has been through such an illness (congestive failure) as this patient had would be much less likely to recover from a second illness such as pneumonia.

DR. J. H. MEANS: I wanted to ask Dr. Lord much the same question,—whether in the face of congestive failure, such as this man had, it was desirable to give serum at all, or whether cardiac failure constitutes a contraindication?

DR. LORD: I would not say it constituted a contraindication in this case, as it is difficult to judge from the description just how ill this patient was. Estimate of the seriousness of illness depends largely on the aspect of the patient and is difficult to put into writing. I would in general say, however, that I think that patients who are already desperately ill and in extremis should not be treated with antiserum. The question then may quite naturally be raised whether statistical studies based on serum-treated cases with the exclusion of the desperately ill compared with a control group not so treated are reliable. In answer to that I would say that observation of this precaution would inevitably introduce a source of error into the figures when no account was taken of the day of the disease in which serum treatment was begun. But the mortality of cases treated with serum within the first few days of the illness is probably not modified to any significant degree, because patients with pneumonia are rarely desperately ill during this early period.

DR. ADAMS: May I add one statement? It seems to me in connection with the changes during the serum reaction that the significant fact is not that the blood pressure dropped to 70/50 but that it dropped from 150/130 down to 70/50. Such a change, particularly in the diastolic figure, is certainly an indication of marked vasomotor upset.

DR. ALFRED KRANES: The blood pressure was not taken immediately before the serum was given. That reading, 150/130, was the admission blood pressure.

DR. ADAMS: I think it is safe to assume that if the pressure was 150/130 when he was admitted and if he improved under treatment, his blood pressure probably did not go down until after the onset of the pneumonia, and that even then it would not have failed so appreciably during the early stages of this complication. One associates such a fall with the final stages of the disease.

Clinical Diagnoses

Hypertensive heart disease.
Arteriosclerosis.
Lobar pneumonia, right middle lobe.
Right scrotal hernia.

Anatomic Diagnoses

Lobar pneumonia, right upper lobe.
Septicemia, pneumococcus.
Acute fibrinous pleuritis with effusion, slight.
Hydropericardium, slight.
Cardiac hypertrophy, hypertensive type.
Chronic vascular nephritis, early.
Adrenal adenoma.

Pathologic Discussion

Dr. Mallory: On the epidemiologic side of the case, we see a considerable number of decompensated cardiacs who pick up in the last few days of their illness an acute bronchitis and sometimes a moderate degree of bronchopneumonia, usually type IV pneumococcus or streptococcus. We do not very often see a true lobar pneumonia as a terminal incident in heart disease. Do you agree with me, Dr. White?

Dr. White: Yes.

Dr. Mallory: So that the appearance of a type II lobar pneumonia must be considered an unusual event in a case of this sort. The fact that the patient in the next bed but one was suffering from the same disease is suggestive, but of course is not proof of contagion.

The autopsy showed entirely what was predicted except for the location of the pneumonia, which was in the upper lobe and not in the lower. Otherwise everything was as we expected.

Dr. White: How much did the heart weigh?

Dr. Mallory: Five hundred grams. The coronary arteries were entirely negative. The kidneys were practically normal in size. There is no question but that it was a pure hypertensive heart disease.

A Physician: Was there any emphysema?

Dr. Mallory: No significant degree of it.

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AUTONOMIC REPRESENTATION IN THE CEREBRUM

IT has long been recognized, since the time of Rokitansky, that the gastro-intestinal tract may be modified pathologically by lesions in the brain. Ulcerations, particularly of the stomach, have occurred in a sufficient number of cases of brain tumor to lead to a neurogenic conception of peptic ulcer. At first the responsibility for this process was placed upon the peripheral vagus nerve; later it was thought the center might be in the medulla, then in the midbrain, and finally it is now recognized by Cushing and others that a lesion of the interbrain may lead to erosions and even acute perforations of the esophagus, stomach or duodenum. It would seem at this level, at least, that there is a station for vegetative impulses that are easily affected by psychic influences, and although this theory, mainly put forward in recent years by Cushing, does not, perhaps, account for all ulcerative processes, it appears to be a reasonable explanation for the majority of them.*

The work which has led to these conclusions has been partly from the clinic and partly from the physiological laboratories. From the latter source a new conception of one of the causative factors in another intestinal disorder, namely, intussusception is discussed in this issue of the *Journal*.† The work has been done in a large series of monkeys in which the motility of the gastro-intestinal tract has been studied in relation to various operations on the cerebral cortex. The area of the brain operation, which was followed by spontaneous intussusception and death in three otherwise healthy monkeys, was a small region in front of the motor cortex now referred to as the "premotor area". This region appears to contain autonomic representation for the gastro-intestinal tract and probably includes both incitatory and inhibitory components.

The work referred to above, on intussusception, is another step in advance in the neurogenic theory of gastro-intestinal disease, the clinical implications of which must be considered as far-reaching. Intussusception in children is by no means a unique disease and is, in most cases, a dangerous cause of intestinal obstruction. If it is sometimes due to cortical dysfunction, as indicated by animal experimentation, a new conception of the subject is at once presented which should lead to further investigation of this important topic.

*Cushing, Harvey. Papers Relating to the Pituitary Body, Hypothalamus and Parasympathetic Nervous System. Part IV. Peptic Ulcer and the Interbrain. Springfield, Ill. & Baltimore, Md.: Charles C. Thomas, 1932.

†Watts, James W. and Fulton, John F. Intussusception—The Relation of the Cerebral Cortex to Intestinal Motility in the Monkey. Page 883.

THE USES OF ADVERSITY

WHEN the Senior Duke of Burgundy, self-exiled in the Forest of Arden, remarked that the uses of adversity are sweet, he was probably using "uses" in its Elizabethan sense of customs or practices. It is not so much the advantages or benefits which men may derive from adversity which are valuable, as the activities and occupations to which they turn, neglected in the piping times of prosperity. Thus, "as from the nettle danger we pluck the flower safety," so from the toad of adversity "ugly and venomous," we may pluck the precious jewel which he is fabled to wear in his head, and which is proof against all other poisons. The modern parallel of this parable of the Duke's is the spirited strip in one of our esteemed and familiar comic contemporaries, entitled, "What to do with the Wolf at the Door."

In common with all his fellow men in this America of the past four years, the doctor has come in for his share of adversity, though no mention has yet been made of any code for his

relief. Happily, like his professional brethren the clergyman and the teacher, he is above the need of a code, or rather he has a code of his own which should fortify him against misfortune and afford ample occupational, if not financial, compensation for the unemployment which the chance of the times may have brought.

The average doctor during the period of so-called depression has seen his practice and income diminish from three principal causes. First, many patients who otherwise would have consulted him, being now so reduced in material circumstances that they cannot afford to do so, go instead to free public clinics, where they obtain excellent advice, care, and service at little or no cost. The enormous recent growth in the clientèle of public medical charitable institutions is evidence of this. Secondly, many of those patients who still consult their private physician rightly expect and demand that his fees shall be much lower than those which they paid willingly a decade ago. Thirdly, many patients fail to pay even the modest fees which the doctor charges, so that his collections fall far below the total of reduced bills which he renders. Thus the average doctor is left wondering how he shall meet his overhead, support his family, educate his children and pay the increased tax on his diminished income.

It is not our present purpose, even were we able to do so, to suggest means of meeting these problems. Rather we would turn attention to some of the "uses of adversity," some of the ways in which the doctor, after solving these problems for himself as best he can, may find occupational advantage for the increased leisure brought him by unemployment.

First, and highest of all, is the privilege which the doctor always enjoys of using his professional knowledge and skill for human service without thought of monetary return. It is the actual exercise of his craft, after all, which affords his greatest satisfaction, his beneficent contact with fellow beings which earns their gratitude and his own happiness.

Secondly, the doctor may find absorbing occupation for leisure, not professionally employed, in his own home and family, if he be fortunate enough to have them. It is characteristic of Americans that they must always go abroad for pleasure and relaxation. It was a successful calamity which first taught the ruined banker to appreciate his own wife and children. So the doctor, formerly so busy that he was never at home, may now learn to enjoy the companionship of his family, to discover what delightful people they really are, to become absorbed in studying astronomy or carpentering with John, in helping Mary with her French or history or music, or even to get out his long disused violin and join the family quartet, though it be as second fiddle. There are always plenty of domestic repair jobs which he can undertake to the joy of his superior four fifths, and to which he can apply the intelligence and mechanical ingenuity which he has acquired in the fields of science. And in his garden, the original habitat and pleasure-ground of the human race, he may find at once, healthful physical labor, aesthetic satisfaction, and perhaps even valuable supplement in produce to the *res angustae domi.*

Finally, it is in the study or by the fireside, that the doctor may find best occupation for his new-won leisure of adversity in reading, marking, and digesting inwardly, not only the medical journalism with which he always feels it his business to keep up, but also the better general literature which he usually neglects. One of the faults of our previously plethoric lives has been that we have let most of our books "fust unused," or rather unperused, on our shelves, so that we have been more familiar with their bindings than their contents. Either Cicero or Pliny, in one of his letters of advice to a young man, wisely and somewhat paradoxically remarks, "It is more important to read the books you own than to own the books you read." This is now the doctor's opportunity, to read the books he owns and thereby make them really his. In this respect our ancestors, with their scanty but well-read libraries, were often better off than we, with our unregarded abundance.

Perhaps we may venture farther hereafter on the subject of the doctor's library. For the present, suffice these suggestions as to some of the uses of adversity which he may find sweeter than at first he is ready to suspect. After all, most of our afflictions generally turn out to be disguised blessings which we have entertained unaware, and inexpensive pleasures prove often the most precious. If he doubt this, let the doctor turn his unoccupied hours to those studies which are at once, "the adornment of prosperity, the solace and refuge of adversity."

DOCTOR WILSON GOES TO NEW YORK

It is always gratifying to know that what we have is desired by others, but not so pleasing when we lose our most valued possessions to them. So it is with the acceptance by Dr. Philip Wilson of the position of Surgeon-in-Chief of the Hospital for Ruptured and Crippled in New York City.

In Boston, Doctor Wilson has made for himself an enviable reputation. With Doctor Cochrane, he has published a textbook on "Fractures and Dislocations" and he is the author of the section on Amputations in the Oxford System of Surgery. He has had the honor of being president of the newly formed American Academy of Orthopedic Surgery. He is an inspiring teacher and has been a productive and skillful member of the Orthopedic Department at the

Massachusetts General Hospital. His personality has endeared him to colleagues and patients alike.

Boston and the Massachusetts General Hospital will regret his transfer to New York, but are glad that he has been offered this larger opportunity, and feel sure that he will repeat, on a greater scale, the success which he has attained in New England.

THIS WEEK'S ISSUE

CONTAINS articles by the following named authors:

WATTS, JAMES W. B.S., M.D. University of Virginia Department of Medicine 1928. Research Assistant (Rank of Instructor), Department of Physiology, Yale University School of Medicine, 1932-1933. Instructor in Neurosurgery, Fellow in Neurosurgery, School of Medicine, University of Philadelphia, Pennsylvania, 1933-. Address: University Hospital, Philadelphia, Pennsylvania. Associated with him is

FULTON, JOHN F. B.S., B.A., M.A., D.Phil., M.D. Harvard University Medical School 1927. Associate in Neurosurgery, Peter Bent Brigham Hospital, 1928. Sterling Professor of Physiology, Yale University, 1930-. Address: 333 Cedar Street, New Haven, Connecticut. Their subject is "Intussusception — The Relation of the Cerebral Cortex to Intestinal Motility in the Monkey." Page 883.

GILLIGAN, D. ROURKE. M.S. Massachusetts Institute of Technology 1925. Research Fellow in Medicine, Harvard Medical School. Research Associate, Medical Research Department, Beth Israel Hospital. Address: Beth Israel Hospital, 330 Brookline Avenue, Boston, Massachusetts. Associated with her is

VOLK, MARIE C. A.B. Radcliffe 1929. Research Assistant, Medical Research Department, Beth Israel Hospital. Address: Beth Israel Hospital, 330 Brookline Avenue, Boston, Massachusetts. And

BLUMGART, HERRMAN L. B.S., M.D. Harvard University Medical School 1921. Visiting Physician, Beth Israel Hospital. Associate Professor of Medicine, Harvard University Medical School. Director of Medical Research, Beth Israel Hospital. Address: 330 Brookline Avenue, Boston, Massachusetts. Their subject is "Observations on the Chemical and Physical Relation Between Blood Serum and Body Fluids. II. The Chemical Relation Between Serum and Edema Fluids as Compared with that Between Serum and Cerebrospinal Fluid." Page 896.

OCKERBLAD, NELSE F. B.Sc., M.D. University of Kansas School of Medicine 1916. F.A.C.S. Professor of Urologic Surgery, University of Kansas School of Medicine. Attending Urologist, St. Luke's Hospital, Kansas City, Mo. His subject is "Some Departures from the Beaten Path in Kidney Surgery. Experimental Studies." Page 906. Address: 1530 Professional Building, Kansas City, Missouri.

PITTMAN, HELEN SINCLAIR. A.B., M.D. Johns Hopkins University School of Medicine 1927. Assistant in Medicine, Massachusetts General Hospital. Her subject is "End-Results in Exophthalmic Goiter. Patients Treated in Pre-Iodine Days." Page 912. Address: 412 Beacon Street, Boston, Massachusetts.

COTTON, FREDERIC JAY, M.D., and MORRISON, GORDON MACKAY, M.D. See page 817, issue of April 12, for records of authors. Their subject is "Flat Foot. An Anatomical Reconstruction." Page 914.

MASSACHUSETTS LEGISLATIVE NOTES

THE VETO OF HOUSE BILL NO. 1305*

The Governor vetoed House Bill 1305 which was designed to authorize the University of Massachusetts Incorporated to grant the Degree of Bachelor of Science. The argument of His Excellency is so cogent that we submit it in full as follows:

The Commonwealth of Massachusetts, Executive Department, Boston, Massachusetts, March 19, 1934.

To the Honorable Senate and House of Representatives:

I am returning without my approval House Bill 1305 entitled, "An Act authorizing the University of Massachusetts Incorporated to grant the Degree of Bachelor of Science." To recognize this university as eligible to grant the degree of Bachelor of Science holds out to the general public that courses of instruction are given, the successful pursuit of which results in a graduate having attained the same scholastic standing as a graduate from the other Massachusetts institutions now granting the degree. As a matter of fact, there is no course of instruction at the University of Massachusetts Incorporated which furnishes the same instruction received by the recipient of a degree of Bachelor of Science graduating from any of the other institutions of learning now granting the degree. This Commonwealth is asked to permit the awarding of a degree of Bachelor of Science in order that the University of Massachusetts Incorporated may set up a course of study in accordance with the recognized educational standards for the degree. In other words, Massachusetts is asked to grant the degree on faith that the institution will conform to recognized standards, and, in my opinion, the authority to grant degrees should not be conferred in that manner. In any event, an analysis of the assets, educational and otherwise, of this institution do (sic) not give sufficient assurance of a maintenance of the high standard which this degree requires to warrant

*The record of the veto is as it appears in House Bill 1338.

the presumption that such standards will be attained if the degree is permitted.

It may be argued that there is an inconsistency in permitting the Staley College of the Spoken Word to grant a degree of Bachelor of Science of Oratory, but this school has for years conducted a course which, in my opinion, entitles it without change of its curriculum to the reward which the State has imposed upon the earnest efforts of the leaders of that institution; while in the instance of this bill, the University of Massachusetts Incorporated has not yet brought its requirements to the customary standards for the granting of a degree of Bachelor of Science. Furthermore, the degree of Bachelor of Science is granted upon an established standard which has been fundamental to it for a long period of time, while the somewhat newer degree of Bachelor of Science of Oratory has not yet the public recognition of scholarship which the degree provided in this bill holds forth.

There is perhaps a more fundamental difficulty with the bill. The name "Massachusetts" has acquired a standard in matters of education recognized throughout the United States and the world. Its use in the conferring of degrees cannot be permitted except in the absence of doubt as to the ability of the institution to meet such educational standard. The Commonwealth itself sustains an educational institution under the name of the Massachusetts State College which, in the course of time, holds the possibility of developing into a university. This is a precious name which in educational matters should be held as the proud possession of the State itself. It should not be appropriated by any private group, however conscientious the intentions of the group may be, which is without endowment or such considerable public support as to guarantee that the institution will maintain the high scholastic standards which the name and the other institutions of the State represent. The title of Massachusetts University properly belongs to the people of the Commonwealth.

For these reasons I am returning the bill without my approval.

JOSEPH B. ELY.

H. 118 was submitted by the Board of Registration in Medicine, and the argument in favor of it was published on page 795 of the issue of April 12, 1934. The action of the Legislature is that "no legislation is necessary". This is an indication that the General Court is not interested in raising the standards of medical practice in Massachusetts. This Commonwealth continues to occupy the unenviable distinction of maintaining the lowest standards relating to medical education in this country. We have been admonished to "have faith in Massachusetts" without a time limit.

MISCELLANY

A SAFETY CONFERENCE

Under the auspices of the Massachusetts Safety Council and Coöperating Organizations, invitations have been issued to attend the First New England Safety Conference and the thirteenth Annual Massachusetts Safety Conference to be held in the Hotel Statler, April 30, and May 1, 1934.

Practically all of the unnecessary hazards to life and health will be dealt with.

The Safety Exhibit will be interesting, and Section 6 on occupational diseases is especially important.

In each of the fourteen sections, matters which concern the medical profession will be discussed. A visit to the Hotel Statler and a study of the program will be worthwhile.

RECENT DEATH

BOUVIER—JOSEPH PETER BOUVIER, M.D., of Whitinsville, Massachusetts, died April 2, 1934 in a Woonsocket, R. I., Hospital, of coronary thrombosis. He was born in La Presentation, P. Q., Canada, on July 16, 1880, the son of Michael and Eleanor (Savage) Bouvier.

His premedical education was received at St. Hyacinth Seminary, Montreal, and he acquired his M.D. degree from Laval University, Montreal, June, 1905, and settled in Whitinsville, Massachusetts, in 1905. He joined the Massachusetts Medical Society through the Worcester District Society in 1930, and was a Fellow of the American Medical Association. He is survived by his widow, Mrs. Eva (Ledoux) Bouvier, and four children, Gabrielle, Simmone, John and Phillip.

REPORTS AND NOTICES OF MEETINGS

BOSTON HEALTH LEAGUE

THE ANNUAL MEETING

On the evening of April 12, 1934, the Annual Meeting of the Boston Health League was held in the rooms of the Twentieth Century Club, 3 Joy Street, Boston. After dinner, the League was called to order by the President, Dr. John W. Bartol, and the following reports were submitted:

REPORT OF EXECUTIVE SECRETARY

During the year 1933 the country again has experienced low mortality and morbidity rates, but "these rates are necessarily based on estimates of the population, and these estimates, in turn, are based on the assumption that the annual increment to the population since the census enumeration of 1930 was the same as that prevailing during the decennium 1920-1930. The latter assumption, however, is open to challenge. Should our population estimates be considerably higher than the true population, all

our calculated rates as now shown are lower than they really are."* The Children's Bureau reports that indications of undernourishment in school children are being received from some parts of the country. Dr. Kleinschmidt of the National Tuberculosis Association has likened our favorable health reports to the free wheeling of an automobile, due to the accumulation of years of work, but he warns us that we cannot roll indefinitely upon this reserve and urges that all health programs be strengthened in order to combat effectively accumulative effects of continued privation which may have serious effects, if every possible effort is not made to offset the depression with sound health program.

COST OF MEDICAL CARE

At the Annual Meeting of the Corporation on March 9, 1933, Dr. Richard M. Smith presented the final report of the Committee on the Costs of Medical Care. Drs. Washburn, Lee, Bigelow, Wilinsky and Bowers discussed briefly the report and it was voted that: "The Executive Committee of the League be directed to consider how it can best serve the interest of the community at this time with regard to the problems connected with the cost of medical care and that it take such steps during the coming year as may seem in its judgment to be wise."

In June at the request of the Hospital Superintendents' Club, the Health League called a meeting for discussion of a plan for prepaid hospitalization, which was attended by hospital superintendents, members of the staff and members of the boards of trustees of the hospitals of Greater Boston. Beyond affording opportunity for discussion of the plan, the League has taken no participation in the project up to the present time, but is awaiting further developments before taking action.

CHILD HEALTH RECOVERY

The only other meeting of the Corporation during the year was a luncheon in October, when Dr. Richard M. Smith and Dr. M. Luise Diez reported on the Child Health Recovery Conference called early in October in Washington by Miss Abbott of the Children's Bureau. It was suggested that any plan undertaken in the State should be a permanent one, and that examinations should be directed toward the control of all aspects of child health and not merely the detection of children requiring relief because of undernutrition.

DENTAL CARE

During 1933 one of the chief concerns of the Health League has been the lack of adequate facilities for free dental care for adults. The eleven dental clinics in ten hospitals or dispensaries and one settlement house reported that during a year less than ten thousand persons received dental care, and this number included children and non-residents of Boston. With more than thirty thousand families receiving Overseer's Aid, and only 12.4 per cent of the total population (781,188 in 1930) under twelve years of age it is clear that these existing facilities are wholly inadequate. A committee composed of representatives of the Metropolitan District of the Massachusetts Dental Society and the Health League considered the situation carefully and a small demonstration has been started for patients able to pay a part of the regular dental fee. These patients are referred by one agency to members of the Metropolitan District of the Massachusetts Dental Society, who have signified their willingness to do this work on a reduced fee schedule. The Committee realizes that this demonstration in no way meets the demand for more free dental work and the problem is still receiving careful consideration.

*Quarterly Bulletin, Department of Health, New York City, Vol. 1, No. 4, 1933.

PNEUMONIA

Because the death rate from lobar pneumonia is rather high in Boston, the Metropolitan Life Insurance Company asked the Health League to sponsor an effort to reduce this mortality. The Health League appointed a medical advisory committee, of which Dr. Frederick T. Lord is chairman, and this committee published a brief article in the *New England Journal of Medicine* asking that physicians report cases promptly to the Health Department and that they avail themselves of the Community Health Association nursing service, if the patient cannot afford a private duty nurse. A letter was sent to each member of Norfolk, Suffolk and Middlesex South Medical Societies, who was practicing within the city limits, calling attention to this article, a reprint of which was enclosed.

CANCER

The Cancer Committee, during the year, has undertaken three definite types of educational lecture work. With the hope of building up informed public opinion, a lecture on the biology of cancer was offered to the colleges of Boston, and was given at Simmons College and the Massachusetts College of Pharmacy, and in both places the students were much interested. Eight lectures were given before mothers' clubs in the settlement houses. The third group to be reached was the nurses at the State Convention in October, when the committee arranged to have Dr. Jackson speak and asked the State Health Department to provide an exhibit on cancer.

One cancer bulletin was published during the year. The leading article was by Clarence Cook Little, Managing Director of the American Society for the Control of Cancer, and was entitled "Biology of Cancer."

SOCIAL HYGIENE

This committee has continued the sponsoring of the Staff Council on Syphilis and Gonorrhea and coöperates with the Massachusetts Society for Social Hygiene in the Boston aspects in a study of social hygiene instruction in the educational system and a proposed institute for nurses.

This committee, at the request of the Committee on the Needs of Ward 9, arranged for a conference with a group of Negro social and church workers,

when Dr. Nels A. Nelson, of the Massachusetts State Department of Health, gave an admirable talk on "The Social Significance of Syphilis and Gonorrhea."

SUMMER CAMPS

The committee this year outlined a well-rounded daily camp routine emphasizing the necessity for sufficient rest. This routine was adopted by the Division of Tuberculosis of the State Health Department and the Massachusetts Tuberculosis League as a standard for the health camps of Massachusetts. The pamphlet was distributed to about 350 persons who are connected with camps, either in the management or in placing children in camps.

USE OF HEALTH MATERIAL

The office of the Health League continues to be consulted frequently in regard to the various health facilities for Boston and morbidity and mortality statistics, and on three occasions the Executive Secretary presented material at meetings. The Federation of Churches asked the Health League to be responsible for the presentation of health material at the Inter-Racial Conference held in April. Graphs showing density of population per inhabited acre and median monthly rental; infant mortality for 1930, 1931, 1932 and the three year average; tuberculosis case rate and tuberculosis death rate for 1930, 1931, 1932, and the three year average by health areas for the city, by census tracts in the South End health area, and by the nine census tracts containing 10 per cent or more Negro population, were shown. Later, the Emergency Planning and Research Board redrafted the graphs which were in color so they could be reproduced in black and white. The Commissioner and the Division of Tuberculosis in the City Health Department, Boston Tuberculosis Association and the Community Health Association have reproductions of these graphs on file in their offices.

The Executive Secretary was also asked to present the tuberculosis graphs at a joint meeting of the Executive Committee and the Health Education Committee of the Boston Tuberculosis Association, and to speak on health trends in Boston at one of the monthly meetings of the settlement house group.

HOSPITAL GUIDE

In order to supplement the information on file regarding hospital beds and clinical facilities in Boston, in November a "Guide for Social Workers Wishing to Secure Free Hospital Care for Clients" was sent to the health and social agencies, who are members of the Boston Health League or the Boston Council of Social Agencies. Many agencies have asked for additional copies and the Guide seems to be helpful in clarifying present policies.

INFANT MORTALITY STUDIES

The three-year graph for infant mortality was also reproduced in the *New England Journal of Medicine* with the infant mortality table by census tracts and health areas for 1932. The three-year average showed very strikingly that the infant mortality rate for Charlestown was in excess of the city rate, while that for the West End was much less. We await with interest the conclusions of the infant mortality study for 1933 of Charlestown and the West End, which is being made by the Harvard School of Public Health and the Bureau of Research of the Boston Council of Social Agencies, under the auspices of a committee appointed by the Health League.

The Health League, in common with all private agencies, was forced to reduce expenditures during the year, but we are grateful for the loyal support of individual subscribers who designated our agency in the Boston Emergency Relief Campaign of 1933 and to the charitable foundations who have made it possible for us to continue our work without curtailing of activities. This review indicates the many topics in which the League has been interested, and to some extent, we hope, the close relationship between the private and public agencies in joint planning. The Executive Secretary wishes to express her gratitude to the Executive Committee, the many special committees of the Health League, and the public and private agencies without whose help it would have been impossible to carry on such a diversified program with so limited a budget.

MARGARET H. TRACY, *Executive Secretary*,
Boston Health League.

REPORT OF THE TREASURER

During the year 1933, the total expenses of the Health League were $5,409.49. The cash balance on January 1 was $250.90. In common with all private agencies, the Boston Health League is experiencing difficulty in financing its program adequately and at the present time is faced with a deficit which will seriously curtail the work during 1934 unless additional funds are forthcoming.

RICHARD G. WADSWORTH, M.D., *Treasurer*,
Boston Health League.

The following officers were elected for the ensuing year:

Honorary President, Francis X. Mahoney, M.D.
President, John W. Bartol, M.D.
Vice President, Rev. Thomas R. Reynolds.
Treasurer, Richard G. Wadsworth, M.D.
Secretary, Charles F. Wilinsky, M.D.
Executive Committee: Gaylord W. Anderson, M.D.; Miss Ida M. Cannon, Mrs. Adolphe Ehrlich, Arthur B. Emmons, 2nd, M.D.; James A. Keenan, M.D.; Horace Morison, Miss Florence M. Patterson, George C. Shattuck, M.D.; Wilson G. Smillie, M.D.; Richard M. Smith, M.D; Frank E. Wing.

At the close of the business meeting Dr. Bartol introduced Dr. Kendall Emerson, Executive Secretary of the American Public Health Association, who delivered an instructive and stimulating address on the "Essential Public Health Services" which will be published in a subsequent issue of this *Journal*.

The paper was discussed by Dr. Henry D. Chadwick, Massachusetts State Commissioner of Public Health.

THE CUTTER LECTURE ON PREVENTIVE MEDICINE

The Cutter Lecture on Preventive Medicine for this year was given on Friday, March 16, at 5:00 P.M. in Building E of the Harvard Medical School, by Dr. Karl Landsteiner, member of the Rockefeller Institute in New York City. His subject was "Immunochemical Specificity."

The speaker was introduced by Dr. Milton J. Rosenau of the Department of Preventive Medicine at the Harvard Medical School. Dr. Landsteiner's pioneer work on the antigen-antibody relationship and his discovery of the human blood groups were briefly mentioned.

After a brief historical survey of the work on the specificity of antigens, especially the proteins, Dr Landsteiner discussed the methods now being used at the Rockefeller Institute. With the development of the inhibition reaction, they have been able to test in detail the immunological specificity of various modified antigens, especially the azo-proteins. The reactions have been found to be the more specific with increasing chain length of the particular modifying group under investigation. Small differences in chemical structure, however, have been shown to produce striking differences in serological reaction. It has even been possible to distinguish cis-trans isomerism such as in maleic and fumaric acids. Considerable work is being done at the present time on the specificity of the antigenic reactions of protein split products, albumoses and proteoses.

Dr. Landsteiner next discussed cellular antigens from the chemical point of view. The significance of the bacterial carbohydrate fractions, as in the pneumococcus, was considered. Carbohydrate as an antigen is probably of importance in tissue cells as well as in bacteria. There is hardly any question but that carbohydrate is capable of arousing immune processes without the aid of protein. The immunizing action of lipoids, however, such as the lecithins, is still very doubtful.

In conclusion, the mechanism of antibody formation was very briefly considered and Dr. Landsteiner compared the process with that involved in the formation of a large complex molecule, like a protein molecule.

THE STAMFORD (CONN.) MEDICAL SOCIETY

The Stamford Medical Society held its monthly meeting at the Stamford Hall Sanitarium on Tuesday evening, April 17. Dr. Graeme M. Hammond, of New York City, read a paper on "Suggestions in the Treatment of Epilepsy," and Dr. William P. Healy presented a paper on "Precancerous Lesions of the Vulva and Cervix," illustrated with slides.

Dr. Frank W. Robertson, Medical Director of Stamford Hall, extended greetings to the members of the Society. Dr. Frank C. McMahon, President of The Stamford Medical Society, presided.

At the conclusion of the meeting, a collation was served to the members of the Society and guests.

BOSTON MEDICAL HISTORY CLUB

The annual meeting of the Boston Medical History Club was held at the Boston Medical Library on Monday evening, April 16. Dr. Merrill Moore read a short paper on "Ulrich von Hutten and Neurosyphilis," and Dr. Ralph C. Larrabee gave a very interesting talk on the attempted ascent of Mt. Washington by Dr. Ball, a Fellow of the Massachusetts Medical Society, in October 1855. Dr. Ball was lost for three days in a very severe storm with his trusty umbrella as his sole companion and lived to tell the tale in his little book entitled the "Perilous Adventure of Dr. Ball."

Dr. Larrabee is an authority on the White Mountains and trail expert of the Appalachian Mountain Club and in 1931 with two companions identified and mapped out the trail of Dr. Ball in his hazardous adventure. This party named the highest point reached by Dr. Ball as Ball's Crag with the hope that it may perpetuate his experience. Dr. Larrabee gave a very graphic account of the perils of the much-underestimated Mt. Washington and illustrated his talk with a large number of stereopticon slides.

The annual report of the Secretary-Treasurer showed a balance of $240.79 after all bills for 1933-34 had been paid, and an active membership of 109. In his report, he called attention to the outstanding programs furnished during the year.

The season began in November, 1933, with the third Medical Historical Pageant by students of Tufts College Medical School under the direction of Dr. Benjamin Spector. In December, Professor Norman E. Himes of Colgate University read an important paper on the "Medical History of Contraception" which was published in the *New England Journal of Medicine*, March 15, 1934. In January of this year, Dr. Henry E. Sigerist, Director of the Institute of the History of Medicine at Johns Hopkins University, gave an informal talk on his trip to Italy in 1933 in search of medieval medical manuscripts. His paper has been published in the Bulletin of the Institute of the History of Medicine, March, 1934. In February, Dr. Francis T. Hunter read a paper on "Mummification" and exhibited x-rays of all the mummies in the Boston Museum of Fine Arts. The March meeting was given over to a symposium on Jewish Medicine based on the manuscripts and books in the "Solomon M. Hyams Collection," and April was reserved for Dr. R. C. Larrabee's very interesting talk on Mt. Washington.

The Secretary commented on the general excellence of the complete program and said that it would be very difficult to duplicate it during the coming year. However, the fourth pageant is assured for November and three very good main papers have been promised for the season of 1934-35 which cares for four of the six regular meetings.

Dr. Charles F. Painter, Chairman of the Nominating Committee, proposed the following names for officers for 1934-35 and all were duly elected:

President: Henry R. Viets, M.D.

Vice-Presidents: Lincoln Davis, M.D.; Hyman Morrison, M.D.; Harold Bowditch, M.D.

Secretary-Treasurer: James F. Ballard.

Council: John W. Bartol, M.D.; Wm. H. Robey, M.D.; Fred B. Lund, M.D.

HARVARD MEDICAL SOCIETY

The Harvard Medical Society met in the amphitheatre of the Peter Bent Brigham Hospital on Tuesday evening, April 10. Dr. L. Stanley Davidson, Professor of Medicine at the University of Aberdeen, spoke on the Incidence, Etiology, and Treatment of Nutritional Anemia.

The meeting was opened with the presentation of two cases of anemia. The first was a boy, 12 years old, who entered the hospital with the history of an enlarged spleen at the age of five. Since last December he had felt ill and complained of a chronic cough. His mother had spent some time in a tuberculosis sanitarium, but had later been discharged "as not having tuberculosis". The boy tired easily, had a temperature of 102° F., had passed dark-colored stools, and had had a gross hematemesis on two occasions. He was, on examination, pale with a rectal temperature of 101° and a pulse of 130. In the midscapular regions there were fine râles on inspiration, and the base of the right lung was flat. A mass in the left upper quadrant extending to the umbilicus suggested an enlarged spleen. Blood examination showed a severe anemia with a hemoglobin of 30 per cent and marked achromia of the red cells. The stools contained occult blood. Pleural effusion was present and the fluid contained 2800 polymorphonuclear cells, 350 lymphocytes, and 350 red blood cells per cubic millimeter, but no tubercle bacilli could be demonstrated. By x-ray there were coarse mottlings of both lung bases. In discussing this case, Dr. Murphy suggested the diagnosis of tuberculosis of the spleen with involvement of the bone marrow. Drs. Minot and Sisson, however, felt that the long duration ruled out this diagnosis and that Banti's disease was more likely.

The second case was that of a woman of 48 years of age showing a marked secondary anemia, due to a neoplasm of the ascending colon which had been surgically removed. Her red cell count on admission had been 3.6 million per cubic millimeter with a hemoglobin of 55 per cent. After treatment the hemoglobin rose to 85 per cent. Dr. Homans stressed the importance of suspecting a neoplasm of the colon when there were local symptoms on the right side of the abdomen with a secondary anemia. When the lesion is in the descending colon there are fewer symptoms.

Dr. Minot introduced Dr. Davidson and stated that King's College, a part of Aberdeen University, founded its medical chair in 1505 and that it represents the oldest foundation for the teaching of medicine in Great Britain. Dr. Davidson stated that all anemias fall into one of three groups: first, those due to a dietary deficiency, directly or indirectly; secondly, those due to a depression of or interference with blood formation; and thirdly, the hemolytic anemias, either congenital or acquired. Of these groups the first is the most important and the most common. It may in turn be divided into two subgroups: first, the macrocytic, "hyperchromic" type for which liver is a specific; and secondly, the iron deficiency anemias where the cells are microcytic and hypochromic. It was with this second subgroup of the deficiency anemias that Dr. Davidson spent the greater part of his time.

Hypochromic anemias are much more common than the hyperchromic (macrocytic) group. Out of a thousand women of the poorer classes at Aberdeen, examined at random, 487 had the hypochromic type while not one had the macrocytic. While the condition does not kill, it leads to a serious lowering of the general vitality with a lowered resistance to infection. Considering the simplicity of the treatment, it is of great importance to recognize the condition.

There are three considerations in the etiology of this defect of the iron metabolism. First, there may be a low iron intake such as occurs from a long-continued milk diet in infants or in the low protein, high carbohydrate diet of the adult. Secondly, there may be defective absorption and the rôle played in this respect by gastric achlorhydria needs consideration. Lastly, there may be an increased demand for iron as in blood loss, pregnancy, or infection.

Among the infants of the working classes studied by McKay in London, 50 per cent showed a hypochromic anemia. At birth the hemoglobin is from 120 to 140 per cent and the red cell count is from 6 to 7 million per cubic millimeter. The reason for this is the low oxygen tension in the blood of the fetus which causes the above compensatory mechanism to take place. At this time the bone marrow is also very active. After twelve weeks the hemoglobin has fallen to about 65 per cent. This fall is a physiological result of the relief of the anoxemia after birth and is directly due to a decrease in the bone marrow activity as well as to an increase of cell destruction. Following this period of fall of hemoglobin content, there is a rise to a somewhat higher level, at which level the normal infant stays. In the child of an anemic mother, however, after the fourth or sixth month, the hemoglobin again falls to about 60 per cent. The cause for this fall is found in the failure of the infant to accumulate the proper amount of iron in his liver before birth, due to the lack of iron in the mother; so that the normal period of low iron intake during nursing is not compensated for by the stored iron. The proper treatment of this condition is with the pregnant mother, although the anemic child can

also be fed iron with excellent results. No matter how anemic the mother may be, the child is always normal at birth, the low hemoglobin not developing until about the sixth month.

In children from four to fourteen years of age the incidence of anemia is less than one per cent, because in this period of life there are seldom extra demands for iron. In the adolescent period, however, chlorosis very frequently used to occur. This happens among young women, especially in the employed classes and presents a pronounced hypochromic anemia. High doses of iron cured it and better diet is perhaps responsible for its decrease. At puberty there is an increase in the body metabolism and menstruation is an added drain on the iron stores and it seems probable that this factor in the face of deficient iron intake played a rôle in the production of this disease which is very rare now. The older clinicians stated that in chlorosis there was often an accompanying hyperacidity, gastric ulcers, and occasional hematemesis, but upon investigation of these beliefs, Dr. Davidson has found that they were not proved by sound experimental or clinical data. The frequency of hypochromic anemia in the middle-aged is astonishing.

In adults, it has been found that the male, unless there is an organic cause, will not develop anemia on as low an iron intake as six to eight milligrams per day. Almost all cases of hypochromic anemia occur in women. Among the poor of Aberdeen nearly 50 per cent of the adult women show some degree of anemia. The first factor of importance is the number of pregnancies, there being two considerations here: first, the fact that the larger the family is the less food the mother will get; and secondly, the added drain of the fetus on the iron supply of the mother. There is a direct relation between the number of pregnancies and the percentage of anemic women in any group. The second factor is the occurrence of achlorhydria (70 per cent of these cases), which may interfere with the utilization of the iron intake. Thirty per cent of the cases showed enlarged spleens; 70 per cent had tongue changes; and 51 per cent had nail changes.

The third factor is the diet. When there are special demands on the iron metabolism of the body, the low intake of six to eight milligrams per day is not sufficient. These people live on a very high carbohydrate diet, 80 to 90 per cent of it consisting of cereals. Yet many do not develop anemia until additional strain, as pregnancy, blood loss, infection, or difficulty in absorption from the gastro-intestinal tract arises.

It is very expensive to correct the diet with regard to the iron intake and the results from such correction are poor. A penny's worth of ferrous chloride or sulphate per day will clear up the condition and act as a preventive measure.

Drs. Minot, Murphy, and Castle discussed the paper, and spoke briefly on chlorosis, the type of iron used, and the proper dosage.

CLOVER HILL HOSPITAL

The next medical meeting of the Clover Hill Hospital will be held in the Reception Room of the hospital at 161 Berkeley St., Lawrence, on Thursday evening, May 3, 1934, at 9 P.M.

The speaker will be Abraham Myerson, M.D., Professor of Neurology, Tufts College Medical School.

His subject will be "The Principal Organic Diseases of the Brain."

All physicians of Lawrence and vicinity are invited to attend.

N. F. DeCesare, M.D., *Chairman.*

HARVARD MEDICAL SOCIETY

The next meeting of the Harvard Medical Society will be held in the Peter Bent Brigham Hospital Amphitheatre (Van Dyke Street entrance), Tuesday evening, May 8, at 8:15 P.M.

PROGRAM

Presentation of Cases.

Factors Controlling the Peripheral Blood Flow in Man. By Dr. Norman E. Freeman.

Studies on the Innervation of the Blood Vessels and Their Application to Neurovascular Surgery. By Dr. James C. White.

Dr. Walter B. Cannon will preside.

John Homans, M.D., *Secretary.*

THE NEW ENGLAND PEDIATRIC SOCIETY

The spring meeting of the New England Pediatric Society will be held in New Haven, Connecticut, on Saturday, May 19, 1934. Details of the program will be published in this *Journal* at a later date.

Gerald Hoeffel, M.D., *Secretary.*

NEW ENGLAND OBSTETRICAL AND GYNECOLOGICAL SOCIETY

The spring meeting of the New England Obstetrical and Gynecological Society is to be held on Wednesday, May 16, 1934, at Portland, Maine.

An extremely interesting program has been arranged.

The registration of members will take place at the Maine General Hospital from 9:00 A.M. until 1:00 P.M., and in the afternoon at the Chamber of Commerce Building, 142 Free Street, from 2:00 P.M. until 5:00 P.M.

Fred J. Lynch, M.D.

FAULKNER HOSPITAL CLINICAL MEETING

The next meeting will be held at the Faulkner Hospital on Thursday afternoon, May 3, 1934, at 5:00 P.M. In addition to the usual clinical pathological conference on the cases which have come to autopsy during the month, Dr. William W. Howell will give a short discourse on "The Infant's and Child's Resistance." All physicians who are interested are cordially invited.

SOCIETY MEETINGS, CONGRESSES AND CONFERENCES

April 26—A Clinic on Pneumonia will be held at 3:30 P.M. in the amphitheater of the Peter Bent Brigham Hospital.

April 27—New England Society of Psychiatry will meet at the Boston State Hospital, Dorchester Center, Mass., at 1 P.M.

April 30—The American Board of Dermatology and Syphilology. Examinations for Certificates. Further information may be obtained from the Secretary, Dr. C. Guy Lane, 416 Marlboro Street, Boston.

May 3—Faulkner Hospital Clinical Meeting. See page 933.

May 3—Clover Hill Hospital. See page 933.

May 8—Harvard Medical Society. See page 933.

May 14, 15, 16, and 17—Thirtieth Annual Meeting of the National Tuberculosis Association. For details apply to the National Tuberculosis Association, 450 Seventh Avenue, New York City.

May 16—New England Obstetrical and Gynecological Society. See page 933.

May 19—The New England Pediatric Society. See page 933.

May 26, 27, 28, and 29—The American Association on Mental Deficiency. Details may be obtained from the Secretary, Dr. Groves B. Smith, Godfrey, Illinois.

June 12—American Heart Association will meet at 9:30 A.M. at the Cleveland Hotel, Cleveland, Ohio.

July 24-31—The IVth International Congress of Radiology will be held in Zurich under the presidency of Professor H. R. Schniz. General Secretary Dr. H. E. Walther, Gloriastrasse 14, Zurich.

September 3-6—American Public Health Association, at Pasadena, California. Dr. J. D. Dunshee, Chairman, Local Committee on Arrangements.

September 4, 5, 6—International Union Against Tuberculosis. For information address the National Tuberculosis Association, 450 Seventh Avenue, New York City.

DISTRICT MEDICAL SOCIETIES

ESSEX NORTH DISTRICT MEDICAL SOCIETY

Thursday, May 3—Censors' Meeting will be held at the Hotel Bartlett, Haverhill, for the examination of candidates.

E. S. BAGNALL, M.D., Secretary.
281 Main Street, Groveland, Mass.

ESSEX SOUTH DISTRICT MEDICAL SOCIETY

Thursday, May 3—Censors' Meeting, at Salem Hospital, 3:30 P.M.

Tuesday, May 8—Annual Meeting. Salem Country Club, Forrest Street, Peabody. Dinner at 7. Speaker to be announced. Subject to be announced.

RALPH E. STONE, M.D., Secretary.
221 Cabot Street, Beverly, Mass.

FRANKLIN DISTRICT MEDICAL SOCIETY

The next meeting will be held on the second Tuesday of May at the Weldon Hotel, Greenfield, at 11 A.M.

CHARLES MOLINE, M.D., Secretary.
Sunderland, Mass.

HAMPDEN DISTRICT MEDICAL SOCIETY

May 3—Censors' Meeting will be held at the Springfield Academy of Medicine, 20 Maple Street, Springfield, at 4 P.M.

HERVEY L. SMITH, M.D., Secretary-Treasurer.
249 Union Street, Springfield, Mass.

MIDDLESEX EAST DISTRICT MEDICAL SOCIETY

The next meeting will take place in May (2nd Wednesday) at Winchester.

ALLAN R. CUNNINGHAM, M.D., Secretary.
76 Church Street, Winchester, Mass.

MIDDLESEX SOUTH DISTRICT MEDICAL SOCIETY

May 3—Censors' Meeting will be held at the Boston Medical Library, 8 Fenway, Boston.

NORFOLK DISTRICT MEDICAL SOCIETY

May—Annual Meeting. Time, place and program to be announced.

FRANK S. CRUICKSHANK, M.D., Secretary.
1695 Beacon Street, Brookline, Mass.

NORFOLK SOUTH DISTRICT MEDICAL SOCIETY

May 3—12 noon at Norfolk County Hospital. Annual Meeting. Election of Officers.

N. R. PILLSBURY, M.D., Secretary.
Norfolk County Hospital, South Braintree, Mass.

SUFFOLK DISTRICT MEDICAL SOCIETY

May 3—Censors' Meeting will be held at 4 o'clock at the Boston Medical Library, 8 Fenway, Boston.

JAMES H. MEANS, M.D., Vice-President.
GEORGE P. REYNOLDS, M.D., Secretary,
311 Beacon Street, Boston, Mass.

WORCESTER DISTRICT MEDICAL SOCIETY

May 9—Annual Meeting. Time and place to be announced later.

ERWIN C. MILLER, M.D., Secretary.
27 Elm Street, Worcester, Mass.

BOOK REVIEWS

Researches Published from the Wards and Laboratories of the London Hospital During 1933. London: H. K. Lewis & Company, Ltd. Price 7s. 6d.

The annual collection of reprints from the London Hospital for 1933 is, as usual, full of splendid material from the laboratories and clinics of this famous institute. Chief among the papers collected in this volume are, first, R. K. Debenham's investigation of 742 cases of haematuria, in which he points out that papilloma and carcinoma of the bladder are the commonest causes in men and inflammatory conditions of the urinary tract the commonest in women. The author is strongly of the opinion that all cases of haematuria should be cystoscoped during the attack of bleeding. Secondly, Arthur Ellis and Horace Evans report twenty cases of renal dwarfism, a rare condition of great interest, first definitely noted thirty years ago by H. M. Fletcher. Thirdly, William Evans also contributes an excellent paper from the cardiac department of the hospital on congenital stenosis of the aortic arch. Lastly, from the department of pathology Dorothy S. Russell writes an excellent review of the subject of the tissue culture of gliomas, accompanied by superb illustrations. These and other papers speak well for the high type of clinical and laboratory research that is carried on at this hospital.

The Interdependence of Medicine with Other Sciences of Nature. By William H. Welch. 48 pp. Baltimore: The Welch Bibliophilic Society, 1934.

In November, 1933, a few friends of Dr. William H. Welch of Baltimore gathered together and formed the Welch Bibliophilic Society. Their object was to publish texts which were unobtainable in such a fashion as met their requirements of taste. The first volume issued by the Society is a reprint of the presidential address given by Dr. Welch at a meeting of the American Association for the Advancement of Science in 1907, not previously available in book form. A pleasant introduction by Fielding H. Garrison points out the value of this work as a contribution to medicine today, "the best study ever made of the interrelationship of medicine and science." This little volume is beautifully printed and bound and is a great credit to this new bibliophilic society. Two hundred and twenty-five copies have been issued privately.